



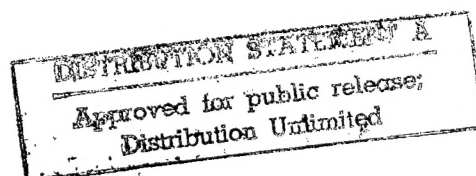
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# ***JPRS Report***

# **Science & Technology**

***Central Eurasia:  
Life Sciences***

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# Science & Technology

## Central Eurasia: Life Sciences

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24 February 1993

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**Effects of Heat Shock and Kartolin-2 on Barley Shoot Growth and Phytohormone Levels**

937C0079B Moscow DOKLADY AKADEMII NAUK  
in Russian Vol 323 No 4, Apr 92 (manuscript received  
13 Jan 92) pp 362-365

[Article by D.P. Yefremov, N.N. Karavayko and O.N. Kulayeva, Institutes of Plant Physiology imeni K.A. Timiryazev, Moscow, and of Biology, Yakutsk Scientific Center, Siberian Branch, Russian Acad. Sci. (manuscript received 13 Jan 92) pp 362-365; UDC 581.3]

[Abstract] An analysis was conducted on the mechanism of action of kartolin-2, an agent known to protect plants from stress. Analysis of roots and runners of Viner [as published] variety of barley showed that treatment of seeds and 72 hour old shoots with kartolin-2 resulted in a ca. 2- to 4-fold increase in abscisic acid levels and almost a 2-fold reduction in zeatin concentrations. Heat shock (45°C for one hour) of 72 hour old control shoots resulted in immediate cessation of shoot growth, followed by a gradual phase of growth resumption. The growth changes correlated with a sharp drop in zeatin levels and a 10-fold increase in abscisic acid levels, followed by a gradual rise in zeatin levels in the face of constant abscisic acid concentrations. Consequently, the effects of kartolin-2 appear to simulate mild stress. In fact, thermally shocked kartolin-2-untreated shoots derived from kartolin-2 treated seeds behaved in the same manner as kartolin-2 treated shoots derived from control seeds. These observations indicate that the hormonal balance had been reprogrammed by kartolin-2 at the seed stage before germination to render the plants more resistant to subsequent stress. Figures 3; tables 1; references 12: 11 Russian, 1 Western.

**Erga-Effect of Vacuoles, Threshold Concentrations of Pollutants, and Probability of Insect Invasion for Coniferous Stands Damaged by Industrial Emissions**

937C0082C Moscow DOKLADY AKADEMII NAUK  
SSSR in Russian Vol 325 No 1, Jul 92 (manuscript  
received 23 Mar 92) pp 198-201

[Article by L. A. Barakhtenova, Z. N. Bryantseva, and I. Yu. Koropachinskiy, Central Siberian Botanical Gardens, Siberian Division, Russian Academy of Sciences, Novosibirsk; UDC 581.1.133.02/07]

[Abstract] The objective of this investigation was to determine the relationship between the accumulation of sulfur and metal oxide pollutants emitted from power plants in Krasnoyarsk Krai in the vacuoles and cell cytoplasm of the mesophyll in coniferous needles and the translocation of the excess of pollutants throughout the plant. The power plant emits 115-125 tons of SO<sub>2</sub> per day; the concentration of SO<sub>2</sub> in the atmosphere is the maximum acceptable; and the fallout of industrial aerosol is 400-500 tons per square kilometer per year. The results showed that the cytoplasm and vacuoles contain identical amounts of Fe and Zn ions, but SO<sub>4</sub><sup>2-</sup>, Mg, Pb, and Cu were found in greater amounts in the vacuoles. The increase in the outflow of absorbed pollutants from the cytoplasm to the vacuole is attributed to the destruction of cytoplasmic structures and a decrease in their sorption capacity. In addition, the increase in the mineralization of the wood tissues weakens the trees and eventually facilitates the settling of the dangerous pest *Dendroctonus micans* Kugel. In conclusion, the results may be used for developing a system for monitoring forest communities damaged by industrial emissions. Figures 2; tables 1; references 8: 7 Russian, 1 Western.

### Kinetic Properties of L-Lysine-2-Monooxygenase From *Pseudomonas putida* and Its Use in Biosensor for L-Lysine

937C0004A Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 27 No 6, Nov-Dec 91 (manuscript received 15 Sep 90) pp 825-832

[Article by A. A. Karyakin, A. K. Strakhova, Ye. Ye. Karyakina, S. D. Varfolomeyev, and A. L. Simonyan, Moscow State University; UDC 577.15]

[Abstract] This work proposes a general kinetic system describing the mechanism of the effect of L-lysine-2-monooxygenase from *P. putida* in solution. A method of polymerization immobilization resulting in the formation of films on the surface of the active element of the transmitter was used to attach the enzyme inside the membrane. It was shown that at an L-lysine concentration of  $2 \times 10^{-3}$  M the reaction rate is directly proportional to the concentration of L-lysine-2-monooxygenase in an enzyme concentration range of  $(0.5-2.5) \times 10^{-7}$  M. The rate of the enzymatic reaction also depends considerably on the nature of the component of the reaction mixture. In addition, the results demonstrated that at pH 8.0-10.0 the rate of the enzymatic reaction was not dependent on the hydrogen ion concentration. Furthermore, it was found that L-lysine-2-monooxygenase is least sensitive to the pH of the medium when the concentrations of the background electrolyte are minimal. Consequently, when using this enzyme in bioamperometric transmitters, it is best to measure in solutions with low ionic strength. It was also shown that the stability of L-lysine-2-monooxygenase increased in response to electroimmobilization of the enzyme in a polyvinyl alcohol gel (8 percent) containing  $10^{-3}$  M L-lysine after treatment with 12.5 percent glutaric aldehyde and also as a result of photoimmobilization. In conclusion, the enzyme electrode based on L-lysine-2-monooxygenase immobilized on the surface of the oxygen transmitter can be used to determine  $10^{-4}$ - $10^{-5}$  M L-lysine. Figures 5; references 14: 6 Russian, 8 Western.

### Use of Luminous Bacteria for Developing Test System for Hexachlorane Cyclohexane

937C0004B Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 27 No 6, Nov-Dec 91 (manuscript received 15 Feb 90) pp 905-910

[Article by L. Yu. Popova, S. Ye. Medvedeva, O. A. Mogilnaya, A. P. Puzyr, and N. S. Pechurkin, Biophysics Institute, Siberian Department, USSR Academy of Sciences, Krasnoyarsk; UDC 504.53.064.2:576.851]

[Abstract] The objective of this investigation was to compare the sensitivity of different strains of luminous bacteria *Photobacterium leiognathi* strains 54, 541, and 542 to hexachlorane cyclohexane (HCCH) under different cultivation conditions. The results showed that strain 541 displayed greater luminous sensitivity to low concentrations of HCCH in contrast to strain 542, due to

more extensive damage to the membrane structures of the cell. The extracellular membrane vesicles and the broken profile of the cell surface and gaps in the external membrane were accompanied by a sharp fall in the level of luminescence. This is a rapid technique, but the lower limit of luminous sensitivity to HCCH makes it inadequate for widespread use of this method. However, it is recommended that strain 541 be used to further increase the sensitivity of a luminous test system for HCCH. Figures 5; tables 1; references 13: 7 Russian, 6 Western.

### Conjugation of 3,4-Benzpyrene and 1,2-Benzanthracene With Plant Peptides

937C0082A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 325 No 1, Jul 92 (manuscript received 17 Mar 92) pp 164-166

[Article by S. V. Durmishidze, D. I. Chrikishvili, and T. V. Devdariani, Plant Biochemistry Institute imeni S. V. Durmishidze, Georgian Academy of Sciences, Tbilisi; UDC 581.19]

[Abstract] This paper presents results on the establishment of pathways for the conjugation of benzpyrene and benzantracene with endogenous cell compounds. Ten-day-old corn and pea shoots were incubated in aqueous solutions of  $7,10^{14}$ C-3,4-benzpyrene and  $9^{14}$ C-1,2-benzanthracene, with specific radioactivities of  $2112 \times 10^4$  and  $2016 \times 10^4$  Bq/ml, respectively, for 24 hours. Subsequent measurements revealed that most (90 percent) of the  $C^{14}$  was located in the roots. The research showed that benzantracene was metabolized more intensively than benzpyrene due to the more steric configuration of benzantracene for the enzymes involved in metabolism. In addition, it was found that peas assimilate and convert both substances better than corn, since the pea roots have active oxidative enzyme systems enabling the hydroxylation of the aromatic ring. Analysis of the radioactive components showed that they are oxy derivatives of benzpyrene and benzantracene. The data also showed that the investigated products of conversion are the products of the conjugation of benzpyrene and benzantracene oxy derivatives with endogenous cell peptides. While the data show that the pathway of conjugation with endogenous peptides plays a considerable role in the biotransformation of benzpyrene and benzantracene in higher plants, in spite of careful research no interesting conjugates with endogenous carbohydrates were found. Figures 1; tables 2; references 12: 4 Russian, 8 Western.

### Expression of Hybrid Gene of Bifunctional Protein 'Insectotoxin-Glucuronidase' in Transgenic Plants

937C0082B Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 325 No 1, Jul 92 (manuscript received 25 May 92) pp 183-186

[Article by A. A. Shchadenkov, S. V. Uzbekova, Ye. V. Kuzmin, T. B. Zolotova, G. I. Eysner, and M. F. Shemyakin, Agricultural Biotechnology Scientific Research

Institute, Russian Academy of Agricultural Sciences, Moscow; Scientific Research Institute of Chemical Means of Plant Protection, Moscow; UDC 577.1]

[Abstract]  $\beta$ -glucuronidase, a popular marker of gene expression, was used to determine the amount of insecticidal protein synthesized in tobacco plants. The tt (codes for a polypeptide corresponding to the toxic fragment of the *Bacillus* protein) and tg (product is polypeptide whose N-terminus corresponds to the toxic fragment of this protein and whose C-terminus corresponds to *E. coli*  $\beta$ -glucuronidase) genes were cloned in the T-DNA of binary vectors pGV941 and pPCV002. The resultant plasmids pGV941H, pGV941tg, and pPCV002tg were inserted into different strains of agrobacteria by direct transformation of bacterial cultures. The *E. coli* glucuronidase gene was inserted into tobacco plants under the control of analogous transcription signals. Extracts of some of the plants were used to determine glucuronidase activity *in situ* in PAAG after electrophoresis. The *Lymantria dispar* caterpillar was used to analyze the insecticidal properties of the resultant transgenic plants. In conclusion, the data indicate the advantages to using the gene for the bifunctional protein "insectotoxin-glucuronidase" in comparison with immunochemical detection of the insectotoxin in transgenic plants. Figures 4; references 8: 2 Russian, 6 Western.

#### Structural Analysis of Protein Component of Black Widow Spider Toxin That Interacts With $\alpha$ -Latrotoxin

937C0084A Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 323 No 1, Mar 92 (manuscript received 17 Dec 91) pp 178-180

[Article by N. I. Kiyatkin, I. Ye. Dulubova, T. M. Volkova, I. A. Chekhovskaya, A. V. Lipkin, and Ye. V. Grishin, Bioorganic Chemistry Institute imeni M. M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 577.112.5]

[Abstract] This study is devoted to the cloning and structural analysis of an 8 kD protein in the black widow toxin that is co-secreted with  $\alpha$ -latrotoxin. These proteins were identified by means of gel chromatography and ion-exchange chromatography. The co-secretion of these two proteins indicated a possible specific interaction between them resulting in the formation of a complex between latrotoxin and the 8 kD protein. The results showed that the amino acid sequence of the 8 kD protein displays no homology to any known proteins. Based on the data, it is assumed that the 8 kD protein makes it possible for the black widow neurotoxin to form channels in lipid membranes. In conclusion, the neurotoxin is viewed as a subunit structure in which latrotoxin is the  $\alpha$  subunit and the 8 kD protein is the  $\beta$  subunit. Figures 2; references 11: 2 Russian, 9 Western.

#### Duodenase—A New Serine Proteinase With Unusual Specificity

937C0085A Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 6, Jun 92 (manuscript received 30 Mar 92) pp 1318-1322

[Article by V. K. Antonov, Corresponding Member, Russian Academy of Sciences, T. I. Vorotyntseva, and T. S. Zamolodchikova, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 577.152.341\*1.01:577.112.083]

[Abstract] In the course of isolating and utilizing enteropeptidases, the authors discovered a new serine proteinase in bovine duodenal mucosa that they named duodenase. Duodenase (MW 29.0 kD) is a glycoprotein containing approximately 3.5 percent sugar (*D*-galactose:*D*-mannose:N-acetyl-*D*-glucosamine 1:8:11). The enzyme is characterized by a high content of the amino acid bases Arg, Lys, and His and, in agreement with this, a high pI value (approximately 9.5). The most remarkable aspect of duodenase is its specificity, which is unusual for serine proteinases. The enzyme exhibits pronounced trypsin- and chymotrypsin-like specificity at pH<sub>opt</sub> 8.0-8.2. Duodenase fairly effectively hydrolyzes oligopeptides such as glucagon, but it does not cleave the Lys-Pro bond. Duodenase's biological role remains unclear. It is interesting to note that the N-terminated sequence of duodenase is to a great extent homologous to the sequences of granzymes (cytotoxic proteases of T-lymphocytes), cathepsin G, and fat cell proteases. Figures 1; references 4: 2 Russian, 2 Western.

#### The Antiacetylcholinesterase Efficiency of Organophosphorus Inhibitors as a Function of Their Phosphorus Atom

937C0112A Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 18 No 4, Apr 92 (manuscript received 3 Jul 91) pp 596-603

[Article by N.N. Shestakova, Ye.V. Rozengart, and B.S. Zhorov, Institute of Evolutionary Physiology and Biochemistry imeni I.M. Sechenov, Russian Academy of Sciences, Saint Petersburg, and Physiology Institute imeni I.P. Pavlov, Russian Academy of Sciences, Saint Petersburg; UDC 577:311\*7.042:547.341.022:539.193]

[Abstract] The molecular mechanics method was used along with a universal conformation program to calculate the stable conformations of 12 organophosphorus acetylcholinesterase inhibitors. Stable conformations were sought by minimizing energy and varying torsion and valence angle values while maintaining constant bond lengths. Conformation energy was represented as the sum of the nonvalence and torsion interactions, the deformation energy of the valence angles, and the cyclization energy. The accessibility of the inhibitors' phosphorus atom for interaction with the nucleophile group in the enzyme's active center was estimated. Conformers whose phosphorus atom is sterically accessible for interaction from the side opposite the breaking



ester bond were selected as productive conformers. A correlation was discovered between the activity of individual organophosphorus inhibitors and their population of productive conformations. Of the organophosphorus inhibitors examined, the ethoxymethyl derivative was found to have the greatest inhibiting effect. Sixty percent of its molecules were in productive conformations. The least active inhibitor examined, i.e., the oxygen-containing analogue, was virtually inactive and contained no conformers. This correlation between activity and population of productive conformations was taken as evidence of the fact that the nucleophile substitution reaction occurs through the formation of an intermediate complex in which the oxygen atom of the serine hydroxyl is located on a continuation of the breaking ester bond. In order for an organophosphorus inhibitor to have an acetylcholinesterase active center, it must have conformers whose phosphorus atom is sterically accessible for interaction from the side  $S_N$ . In order for this to occur, the structure of the entire phosphoryl group (including the substituents at the phosphorus atom from the side of the attack vector) should be nearly planar. Figures 2, tables 5; references 14: 8 Russian, 6 Western.

#### New Biologically Active Substances of Protozoa and An Assessment of Their Action

937C0133A Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 6, Nov-Dec 91 [manuscript submitted 21 Mar 91] pp 838-856

[Article by N. N. Sukhareva, V. M. Urinyuk, M. M. Vyadro, S. M. Navashin, Moscow State University imeni M. V. Lomonosov, Biology Department; All-Union Science Center for Antibiotics, Moscow; UDC 576.8:576.809.7]

[Abstract] The search for novel producers of highly selective biologically active substances with low toxicity has thus far focused little on protozoa, which are only gradually finding a place among the traditional targets of biotechnology, i.e., bacteria, fungi, and algae. The researchers here note that flagellates synthesize certain biologically active substances inherent to animals and plants and not found in prokaryotes. In addition, some protozoa having metabolic dualism are capable of producing substances typical of both plants and animals. The first protozoan preparations were lysates or extracts of *Trypanosoma cruzi*. Since *T. cruzi*, however, is pathogenic for humans and needs a complex, expensive medium for cultivation, these researchers chose for their study nonpathogenic trypanosomides *Crithidia oncopelti* and *Trypanosoma lewisi* and the flagellate *Astasia longa*. They studied the composition and biological activity of the total lipid fraction of those species, sucrose ethers and fatty acids (*A. longa*), reserve  $\beta$ -1,3-glucane of *A. longa*, and a fraction of the surface glycopospholipids and peptides of *C. oncopelti*. It was demonstrated that three types of chemically different protozoan preparations produced exhibit a pronounced activating effect on

macrophages, have a preventive effect in terms of bacterial infections in mice with solid tumors, and show pronounced antimetastatic action against pulmonary metastases. Those properties, as well as antitumor and immunomodulating action and the absence of toxicity, make astasilide, astasian, and the surface glycopospholipid/peptide preparation a new group of protozoan biological-response modifiers. Figures 4, references 72: 43 Russian, 29 Western.

#### Effect of Phenyl Derivatives of Glutaminic and Aspartic Acids on Neuromuscular Transmission in Locust *Locusta migratoria*

937C0133B Moscow ZHURNAL EVOLYUTSIONNOY BIOKHIMII I FIZIOLOGII in Russian Vol 27 No 5, Sep-Oct 91 [manuscript submitted 1 Feb 91] pp 621-624

[Article by Yu. Ye. Mandelshtam (deceased), N. A. Anisimova, T. V. Vovk, L. I. Deyko, S. V. Ivlev, I. B. Lapshina, V. V. Perekalin, Institute of Evolutionary Physiology and Biochemistry imeni I. M. Sechenov, USSR Academy of Sciences, Leningrad; Leningrad State Pedagogical Institute imeni A. I. Gertsen; UDC 591.182:595.727]

[Abstract] Although earlier research by this group demonstrated that aliphatic esters of glutaminic acid are capable of blocking glutamate receptors, the action of those substances on neuromuscular synapses of insects was not very specific and was easily reversed. Here the researchers focus on whether the blocking action of the esters of excitatory amino acids can be enhanced by inserting a cyclic element into the molecule. Using  $\beta$ -phenylglutaminic acid and  $\beta$ -phenylaspartic acid, plus symmetric esters of those acids — diethyl, diisopropyl, and diisobutyl esters—as well as para-, meta-, and orthoisomer phenylene dialanines and diethyl and diisobutyl esters of  $\beta, \beta'$ -(paraphenylene)-dialanine, they registered the effects produced on muscle fibers of muscle 120 (Snodgrass) of *Locusta migratoria* L. The activity of the compounds was ascertained on the basis of the magnitude of the concentration required for reducing the amplitude of excitatory postsynaptic potentials or glutaminic potential by 50 percent of their initial levels. Most of the phenylaspartic acid and phenylglutaminic acid esters, as well as the diisobutyl ester of the  $\beta, \beta'$ -(paraphenylene)-dialanine, were found to block the neuromuscular synapses and reduced the potentials and the glutamate depolarization responses of the fibers. Only in the presence of the diisobutyl ester of phenylaspartic acid did the amplitude of the excitatory postsynaptic potential and of the glutamate responses increase. The latter phenomenon, it is speculated, stems from a complex of features of molecular structure: aspartic base, isobutyl ester radicals, presence of phenyl in  $\beta$  position. Figures 2, references 7: 3 Russian, 4 Western.



### Protein-Engineering Studies of Visual Rhodopsin

937C0119A Moscow *SENSORNYYE SISTEMY*  
in Russian Vol 6 No 3, Jul-Sep 92 (manuscript received  
25 Feb 92) pp 74-77

[Article by T.A. Zvyaga, V.V. Gurevich, I.D. Pokorvskaya, M.N. Garnovskaya, I.L. Dumler, Ye.P. Tserf, and S.A. Zozulya, Pushchino Affiliate, Bioorganic Chemistry Institute imeni M.M. Shemyakin, Russian Academy of Sciences, and Evolutionary Physiology and Biochemistry Institute imeni I.M. Sechenov, Russian Academy of Sciences, Saint Petersburg; UDC 612.843.142]

[Abstract] Visual rhodopsin, which is the primary acceptor of light in Eukaryotae, is a representative of a large family of membrane receptors that are conjugate with G-proteins, have a similar structurofunctional organization, and play a key role in the processes of the reception, transformation, and transmission of light, hormonal, and neuromediator signals. Two exceptionally conservative negatively charged amino acid residues of the second and third transmembrane domains, i.e., Asp83(II) and Glu134(III), are especially interesting. Previous studies have demonstrated that the spectral properties of mutagenic bovine visual rhodopsin Asn83 and Glu134 are in no way different from the wild type of rhodopsin. Whether these mutants are capable of activating the effector enzyme phosphodiesterase cGMP has not previously been established, however. The functional activity of two mutagenic forms of bovine visual rhodopsin, i.e., Asn83 and Glu134, was therefore studied. A eukaryotic acellular translation in a wheat germ extract was used to express the recombinant rhodopsin and its mutagenic forms. The expression level of recombinant opsin in the acellular translation amounted to 30-40 µg protein per milliliter of translation mixture. Between 15 and 20 percent of the synthesized opsin was incorporated into phosphatidyl choline liposomes by countertranslation and amounted to more than 12 percent of their total protein content, thus permitting functional testing of the recombinant rhodopsin incorporated into the liposomes without any further purification. The data obtained in testing the functional activity of the study forms of visual rhodopsin in five independent experiments confirmed that the substitutions Asp83 → Asn and Glu134 → Gln did not significantly alter rhodopsin's ability to stimulate the GTPase activity of transducin as compared with the wild type of recombinant rhodopsin. Its ability to activate the effector enzyme cGMP phosphodiesterase was nevertheless completely destroyed. The study results were entirely consistent with literature data regarding analogous mutagenic forms of other receptors conjugate with G-proteins. It was hypothesized that the residues studied

participate in a process of additional receptor-dependent activation of G-protein (transducin) other than catalysis of nucleotide exchange on its  $\alpha$ -subunit. Figure 1; references 9: Western.

### The Secretion of Recombinant hEGF Into Periplasm in *E. coli* Cells

937C0112B Moscow *BIOORGANICHESKAYA*  
*KHIMIYA* in Russian Vol 18 No 6, Jun 92 (manuscript  
received 19 Sep 91; after revision 27 Jan 92) pp 766-776

[Article by N.V. Batchikova, I.B. Altman, S.V. Lutsenko, V.A. Smirnov, I.V. Nazimov (Bioorganic Chemistry Institute imeni M.M. Shemyakin, Russian Academy of Sciences, Moscow), L.G. Eshkind, Ye.A. Sinyagina, and A.V. Azhayev, Khimtek Small Joint Enterprise; UDC 577.122]

[Abstract] A series of secretion vectors was constructed in which a synthetic gene of epidermal human growth factor [hEGF] spliced to the gene coding the leader peptide of one of the major proteins of the outer membrane of *Escherichia coli*, i.e., OmpF, is controlled by the promoter  $P_{tac}$  pKKD plasmid containing a  $P_{tac}$  promoter whose polylinker segment and *rrnB* gene transcription terminator represented modified pKK223-3 (Pharmacia) commercial plasmid was used as a vector. The modification of the said commercial plasmid included eliminating the *Bam*HI and *Sal*I retranscriptase sites in the segment coming from pBR322, as well as replacing a portion of the polylinker by a synthetic sequence in which an *Xho*I site appears instead of the *Eco*RI, *Sma*I, and *Bam*HI restrictase sites while the *Pst*I and *Hind*III sites are preserved. pBT-hEGF plasmid and *E. coli* of the JM105 strain were used to produce a periplasmatic fraction from which the target protein was obtained in analytical quantities by sorption on a minicolumn with SepPack C18 and by high-performance liquid chromatography. The target protein was isolated in a nearly homogeneous (>98 percent) state in a yield of 7 mg/l bacterial culture. The N-terminal amino acid sequence (25 amino acids) of the resultant hEGF was found to correspond to the natural hEGF sequence. The hEGF produced was determined by SDS-electrophoresis to have a molecular mass of 7 kDa. The hEGF preparation isolated was determined to possess a pronounced biological activity in a test involving opening the eyes of neonate mice. Those mice that did not receive any injections opened their eyes on day 14, whereas those injected with mEGF opened their eyes on day 8 or day 9 and those injected with hEGF opened their eyes on day 10 (which is consistent with literature data for natural hEGF). The studies performed established that the yield of target product may be increased by increasing copies of the recombinant gene. Figures 5, tables 2; references 18: 3 Russian, 15 Western.

**Study of Antigen Structure of HIV by Using Synthetic Peptides**

937C0112C Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 18 No 6, Jun 92 (manuscript  
received 17 Dec 91) pp 784-793

[Article by V.S. Ivanov, L.D. Chikin, Z.K. Suvorova (Central Scientific Research Institute of Epidemiology, Moscow), A.T. Kozhich, and V.T. Ivanov, Bioorganic Chemistry Institute imeni M.M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 578.825.083.3]

[Abstract] A series of more than 40 synthetic peptides were used in an effort to find antigen determinants of HIV-1 and HIV-2. Specifically, likely antigen determinants of proteins coded by the genes *env*, *gag*, *pol*, and *nef* were sought. The peptides were synthesized by the solid-phase method. Liquid hydrogen fluoride purified by reverse-phase high-performance liquid chromatography was used for deblocking and removal of the peptides from the resin. The synthesized peptides were characterized by amino acid analysis, FAB-mass spectrometry, and analytical reverse-phase high-performance liquid chromatography. Indirect solid-phase immunoenzyme analysis with the peptides serving as antigens was used to estimate the peptides' reactivity with respect to serum containing HIV-1 and HIV-2 antibodies. Only two synthetic peptides were found to be promising for use in the early diagnosis of HIV; a third synthetic peptide reacted to one of the nine serum samples on one of the two test panels used and was thus determined to have only dubious promise as a diagnostic tool. The three synthetic peptides showing reactivity were used to make a composite that was in turn used to develop a diagnostic test system for detecting HIV-1 and HIV-2 antibodies. Tables 3; references 39: 5 Russian, 34 Western.

**A Study of the Amino Acid Sequence of the Black Widow Spider Venom Latroinsectotoxin**

937C0112D Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 18 No 6, Jun 92 (manuscript  
received 29 Dec 91) pp 871-874

[Article by O.V. Bulgakov and V.N. Pashkov, Pushchino Affiliate, Bioorganic Chemistry Institute imeni M.M. Shemyakin, Russian Academy of Sciences, Pushchino, Moscow Oblast, and T.M. Volkova, T.G. Galkina, K.A. Pluzhnikov, and Ye.V. Grishin, Bioorganic Chemistry Institute imeni M.M. Shemyakin, Russian Academy of Sciences, Moscow; UDC 577.112.5:595.44-114.52.088]

[Abstract]  $\alpha$ -Latroinsectotoxin isolated from the venom of the black widow spider (*Latrodectus mactans tredecimguttatus*) was subjected to structural analysis. The  $\alpha$ -latroinsectotoxin isolated was determined to be a protein with a molecular mass of about 120 kDa. Its N-terminal amino acid residue was determined to be glutamic acid, and its amino acid composition was found to be consistent with that described previously. The protein preparation isolated had a paralytic effect on the mouse *Musca domestica*. The following N-terminal amino acid sequence of  $\alpha$ -latroinsectotoxin was determined by analyzing preimmobilized protein: Glu-Met-Ser-Xaa-Ala-Asp-Gln-Xaa-Lys-Leu-Leu-Ala-Tyr. Further structural studies of the  $\alpha$ -latroinsectotoxin were then performed to obtain data to clone its structural gene. The toxin was digested by trypsin, and total or partial amino acid sequences of 26 tryptic peptides were established. Several of the peptides were found to possess significant structural similarities with segments of the latrotoxin molecule, and three peptides were found to actually coincide with latrotoxin segments containing internal structural repetitions that likely play an important role in the manifestation of the functional activity of both toxins. Figures 2; references 4: 1 Russian, 3 Western.

**Hypoxygenation in Chronic Cs-137 Carriers:  
Gray Vole (*Clethrionomys glareolus*) Studies**

937C0078B Moscow DOKLADY AKADEMII NAUK  
in Russian Vol 324 No 5, Jun 92 (manuscript received  
18 Apr 92) pp 1125-1127

[Article by T.P. Krapivko and A.I. Ilyenko, Institute of  
Animal Evolution and Ecology imeni A.N. Severtsov,  
Russian Acad. Sci., Moscow; UDC 577.4]

[Abstract] An analysis was conducted on oxygen uptake  
in gray vole (*Clethrionomys glareolus*) populations in the  
Mogilev Oblast of Belarus exposed to high radionuclide  
levels since the 1986 Chernobyl accident. Such animals  
have been identified as chronic carriers of Cs-137 (90.4  
Bq/g). Earlier studies had shown that oxygen uptake in  
the 2d generation (1986) of exposed voles (5.2 ml/g/h of  
O<sub>2</sub>) was lower than in control voles (5.62 ml/g/h of O<sub>2</sub>).  
The same level of diminished uptake (5.16 ml/g/h of O<sub>2</sub>)  
was observed in the 12th generation in 1991 in the  
chronic Cs-137 carrier populations. Since reduced  
oxygen consumption has been demonstrated to offer  
protection against radiation sickness in a variety of  
model systems, the present findings on reduced oxygen  
consumption in the at risk vole population appear to  
reflect adaptive mechanisms intended to mitigate radia-  
tion damage. Figures 1; tables 2; references 2: Russian.

**Environmental Aspects of Thallium in  
Diamond-Rich Vilyuy River Region of Yakutia**

937C0078C Moscow DOKLADY AKADEMII NAUK  
in Russian Vol 324 No 5, Jun 92 (manuscript received  
17 Mar 92) pp 1128-1130

[Article by V.K. Marshintsev, R.N. Kopylov, V.G.  
Shirman and S.M. Zakharova, Institutes of Applied  
Ecology of the North and of Mining in Northern  
Regions, Yakutsk Scientific Center, Siberian Depart-  
ment, Russian Acad. Sci.; UDC 546.683.552.323.6  
(571.56)]

[Abstract] An environmental assessment was made of  
thallium as a component of the ecosystem in the Vilyuy  
River region in Yakutia, an area renown for its diamond  
deposits. The results showed that thallium represents a  
serious health hazard in view of its high toxicity and  
extensive presence in soil, water, and snow samples. This  
situation is due to a large extent to extensive diamond  
mining, recovery, and processing operations. Environ-  
mental pollution with thallium results directly from its  
use in heavy-liquid sink-flot solutions for gravity isola-  
tion of diamonds, as well as from the fact that the  
average thallium levels in kimberlite in that area are on  
the order of 0.29 g/ton. Tables 2; references 3: Russian.

**Further Research on Extraction of <sup>134</sup>, <sup>137</sup>Cs From  
Animal Meat**

937C0083A Moscow DOKLADY AKADEMII NAUK  
SSSR in Russian Vol 324 No 2, May 92 (manuscript  
received 20 Mar 92) pp 484-486

[Article by A. I. Ilyenko and T. P. Krapivko, Institute of  
Evolutionary Morphology and Ecology of Animals imeni  
A. N. Severtsov, Russian Academy of Sciences, Moscow;  
UDC 581.5]

[Abstract] Various decontamination solutions were used  
to extract <sup>134</sup>, <sup>137</sup>Cs from the meat of wild boar (*Sus  
scrofa*), moose (*Alces alces*), pike (*Esox lucius*), tench  
(*Tinca tinca*), roach (*Rutilus rutilus*), and crucian carp  
(*Carassius carassius*) trapped in Belarus. The wild boar  
and moose meat had specific radioactivities of 5.9x10<sup>-8</sup>  
and 8.5x10<sup>-8</sup> Ci/kg, respectively. The meat was frozen  
solid, thawed, then cut into pieces, and the experiments  
were performed at room temperature. The data showed  
that after three hours of washing 45.8 percent of the  
radionuclide was removed from the wild boar meat and  
71.8 percent from the moose meat. In addition, it was  
shown that seven water changes over a period of 10.5  
hours removed 96.8 percent of the radionuclide from the  
pike. The results showed that increasing the frequency of  
changing the decontamination solution decreases the  
total decontamination time necessary for meat and fish  
by two-fold. In addition, adding KMnO<sub>4</sub> to the decon-  
tamination solution significantly accelerates the washing  
of cesium radionuclides. And finally, freezing fish and  
meat increases the effectiveness of decontamination.  
Tables 3; references 4: Russian.

**Reasons for Decrease in Amudarya Discharge  
From Its Origin for 1961-1985**

937C0083B Moscow DOKLADY AKADEMII NAUK  
SSSR in Russian Vol 324 No 2, May 92 (manuscript  
received 13 Jan 92) pp 487-491

[Article by N. A. Shilo and M. I. Krivoshey, Institute of  
Ore Deposits, Petrography, Mineralogy, and Geochem-  
istry, Russian Academy of Sciences, Moscow; UDC  
551.482.215.1]

[Abstract] This paper examines whether a decrease in  
water inflow from the origin of the discharge is actually  
associated with climatic factors. The data showed that the  
distinct negative trend in the multi-year course of the  
inflow for 1961-1985 does not agree with precipitation,  
which has a positive trend. They also showed that the  
decrease in discharge can in no way be attributed to  
precipitation. In addition, for 1961-1985 the air tempera-  
ture in the warm period increased by 1°C, which would  
have increased discharge due to glacial melt, so the  
decrease in discharge cannot be attributed to climatic  
factors. The data showed that deviations in discharge from  
the curve of regression are closely associated with the  
magnitude of strong earthquakes whose epicenters are  
located within 100 km of the river bed. In conclusion, the  
results suggest that the decrease in Amudarya discharge at

its origin is due to filtration losses in the river bed as a result of seismic activity rather than climatic factors. Figures 3; tables 2; references 2: Russian.

### **Hydrobiological Research in the Arctic: Plant Communities in the Spitzbergen Archipelago (Western Part)**

937C0085B Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 6, Jun 92 (manuscript received 25 Mar 92) pp 1332-1335

[Article by V. B. Vozzhinskaya, M. M. Bolduman, V. V. Pestrikov, and A. L. Sorokin; presented by Academician M. Ye. Vinogradovyy 25 Mar 92; Institute of Oceanology imeni P. P. Shirshov, Russian Academy of Sciences [RAN], Moscow; Polar Scientific Research Institute of Fisheries and Oceanography, Archangel; UDC 591.9(26)+581(268.4)]

[Abstract] In the late 1980's, scientists from the Expedition of the Institute of Oceanology and the Polar Institute of Fisheries and Oceanography conducted research on the structure of benthic communities and the feasibility of utilizing individual types of invertebrates and algae on the west coast of West Spitsbergen Island. Work was conducted at stations and on ships (SRT [medium fishing trawler] "Poisk," SDYe "Kama") by means of trawling and underwater submersion in light diving equipment. Trawling was conducted at depths of 3-5, 10-12, 15-20, 30-35, and 45-50 m, and submersions at 15 m. In 1989, 18 profiles from the water's surface to a depth of 50 m were constructed and in 1990, 26; in all, more than 600 data sets were collected. Scientists K. L. Vinogradova, V. S. Kuzin, N. S. Peltikhina, S. V. Cherkashin, V. O. Mokiyeyskiy, and K. R. Tabachnik from the Institute of Oceanology, RAN; Botany Institute, RAN; and Polar Institute of Fisheries and Oceanography collected the data, taking 1450 samples. They discovered 66 types of algae (8 green, 29 brown, and 29 red) of which 14 types of macrophytes were new for this archipelago. The presence of a well developed zone of benthic plant life (based on laminarian algae) showed that coastal ecosystems in this region of the high Arctic function normally and can serve as a basis for ecological monitoring in arctic latitudes. Figures 2; references 5: 3 Russian, 2 Western.

### **On an Ecologically Differentiated Approach to Studying Bioaccumulation of Chemical Elements and Compounds in Marine Organisms**

937C0085C Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 6, Jun 92 (manuscript received 7 May 92) pp 1336-1338

[Article by A. P. Kuznetsov, L. L. Demina, and I. P. Shmelev; presented by Academician V. Ye. Sokolovyy, 6 May 92; Institute of Oceanology imeni P. P. Shirshov, Russian Academy of Sciences, Moscow; UDC 577.4]

[Abstract] In this work, the authors compiled data from previously published works on bioaccumulation of transition metals in benthic invertebrates in various ocean regions (North and South Atlantic, Sea of Japan, etc.) and undertook an ecologically differentiated approach to studying the content and degree of accumulation of metals (Fe, Mn, Ni, Co, Cu, Zn, Pb, etc.) in benthic organisms of those regions. The metal content in animals was studied in a comparative scheme with respect to metal content in the benthic sediments in which those animals lived and utilized the sediments' organic matter and heterotrophic and autochemolytrophic bacterial populations as food. The accumulation coefficients were calculated by the following equation: metal content in the organism/metal content in sediment, which yielded values several orders of magnitude smaller than those normally calculated on the basis of metal content in seawater. The authors argued that seawater-based accumulation coefficients may be useful for pelagic organisms but that they are meaningless for benthic organisms that live in or near the sediment, i.e., accumulation coefficients must be differentiated to account for the specific environments in which different organisms live. The authors showed that accumulation coefficients varied with the organisms' proximity to hydrothermal sources and stressed that one of the primary causes for changes in the distribution of life on the planet is changes in the geochemistry of the earth's surface. References 6: 4 Russian, 2 Western.

### **Ecological Work of World Laboratory in Russia**

937C0106B Moscow POISK in Russian 31 Jul 92 p 13

["Modest Appeal of Expert Investigation". First two paragraphs are POISK introduction in boldface.]

[Text] Today we are concluding the publication of a series of materials on the more interesting projects of the World Laboratory in Russia.

In their time the specialists of the International Ecological Environmental Monitoring Station (IEEMS) conducted ecological expert investigations of the production of uranium and beryllium at the Ulbinsk Metallurgical Plant in Ust-Kamenogorsk. At that time in the conclusion they described the extreme danger, especially to local residents, of the inadequate safety measures. There was an accident one year later, and a beryllium cloud hung above the city. "We warned you," repeated the director of the IEEMS, professor Grigoriy Barenboym.

IEEMS was born of ecological chaos.

On the one hand there was the horrifying condition of the environment, which western writers call the result of "ecocide in the USSR". All of its components—air, land, water, and food—were contaminated with a multitude of toxic substances (for example, more than 150 toxic substances have been found in the air of Kemerov, and nearly 100 have been found in the water. And even when

the notorious maximum acceptable quantity levels are normal taken alone, when combined they make a truly hellish mixture.

On the other hand, there are the inconsistency in methods and the fragmentation of the agencies occupied with assessing the pollution (measuring), which is performed mechanically and not correlated with the diseases of the people and their quality of life.

The first foothold in the attempt to subdue this chaos to common sense was the concept of "ecological risk". Having taken this as the basis, Barenboym and his colleagues associated descriptions of the environment with characteristics of biological objects, primarily man. Based on the experience of many expert investigations, they asserted that simply stating the fact that "it's bad in this region" would only exacerbate public stress. It was necessary to learn how to control the situation and for this purpose different scenarios for its development were simulated (for example, the construction of a new factory, or the start-up of purification installations, or the placement of additional filters will be reflected—in figures—on the infant morbidity level). Based on the prognoses, we make expert conclusions on what to build and what to close.

"With the advent of perestroyka," says Barenboym, "we felt a sharply increasing demand for expert investigations as a source of correct information. But not just any expert investigations, only independent ones, which in the opinion of the citizens could only be international expert investigations. The World Laboratory, which has broad science contacts, helped us organize it."

Arising in 1989 under the wings of the department of the World Laboratory, the station employed another, novel for that time, opportunity to sign contracts with our specialists without taking them away from their primary work.

Barenboym first gathered ecologists from different establishments in the Kuzbass. There they organized a separated water expert investigation, having invited the most outstanding French specialists. The Paris Center for Water Quality Control performed the analyses, each of which cost 1,100 dollars, at no charge. The series of expert investigations made it possible to identify one of the key problems in the Kuzbass, the hazard drinking water presents to man. Work has begun on improving the water, and local authorities have already built bridges themselves with western firms.

The expert investigation, which was also repeated and international, "revealed" the large scale production of polyvinyl chloride in Irkutsk Oblast. Then the scientists were sent to Ust-Ilimsk, where a dramatic collision was taking place: the timber industry complex was polluting the Angara [River] and the public was opposing the construction of a yeast hydrolysis factory that could refine many wastes.

From there the international team with the streamlined technique of analyzing samples in our laboratories and foreign ones went to Latvia. The government there had given orders to close the Slokskiy Cellulose-Paper Factory.

Today Barenboym responsibly claims that this was the policy and is still the policy: they strived to place all the ecological sins of the beach health resort on the "Russified" factory: both the fumes from the fire-rooms, which burn the coal contaminated with toxic elements and the automobile exhausts in Yurmala, and the antiquated refineries in Riga, and the wastes from the chemical plants in Liyelup. A detailed report was prepared with the participation of the French and Germans. As a result, the factory, which was able to correct the problems, is operating successfully. The republic needs it...

No less difficult were the expert investigations of the Astrakhan condensed gas complex, the aluminum plant in Tadzhikistan, Moscow drinking water...

It was found that the single visits of even prominent guests were not effective; you won't get objective data in a hurry (the wind direction changed, toxic production was temporarily concealed, meetings were specially organized for the arrival of the commission).

The IEEMS began to open its centers in the bad cities. A network of independent monitoring stations was set up. We began to see elements of order in the chaos.

During their trips to all the cities the scientists became convinced that many disasters occur as a result of the ecological illiteracy of the public and the power of those in authority. Expert investigations alone will not help here. In the first year of the creation of the IEEMS an ecological school was held in Pereslavle-Zalesskiy for 200 children and 200 adults from the republics, the United States, Canada, Belgium, and France. Student summer laboratories are held each year.

Thus, harmony has also been added to ecological education; its crown will be the higher international ecological school. Four of its departments will train specialists in complex expert investigations, international ecological policy, ecological problems of disarmament, and leaders of nature protection groups.

We should not be surprised that IEEMS, which encompasses expert investigations from almost half of the country, has a good reputation in the West. Such celebrity does not go "unpunished": the station has been assigned the role of coordinator in the international project "Global Ecological Monitoring". An idea expressed by Edward Teller at one of his seminars involves using the observation subsystem "Brilliant Eyes" of the SDI system for the needs of ecology. After two years of tense preparation, it took actual form and will be embodied on three levels: ground, aviation, and space. It is the largest project in the history of the World Laboratory.



**Population Aspects of Adaptation of Hydrobionts to Toxic Factors**

937C0135A Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 4, Oct-Dec 91 [manuscript submitted 14 Feb 91] pp 34-41

[Article by L. D. Gapochka, M. Battakh, T. S. Drozhzhina, G. A. Karaush, O. B. Shavyrina, T. I. Belaya; UDC 574:23.574.632]

[Abstract] Analysis of hydrobiont population response to pollutants is important to the development of means of forecasting the state of water ecosystems. Such analysis, however, is impossible without a technique that enables examination of the response of the population as a single biological system. A convenient model for such research is a population of single-celled organisms that represent unique genetic systems. The researchers here present information on the features of populations of the green algae *Scenedesmus quadricauda* Breb. and the infusoria *Spirostomus umbiquum* Ehrbg. var. major. exposed in culture to copper and phenol. They found that the toxins lead to a more rapid population formation in the green algae, with an increase in the toxic resistance of the algae, a phenomenon directly linked to the fact that there were more cells. With the infusoria, rapid population growth did not occur, and resistance, as with the algae, varied with culture age. It was, however, independent of population size. Figures 5, references 9: Russian.

**Distribution of Heavy Metals in Phylloid Tissue of Brown Alga *Sargassum pallidum* (Turn.) S. Ag.**

937C0135B Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 4, Oct-Dec 91 [manuscript submitted 22 Nov 90] pp 41-45

[Article by Ye. Yu. Zolotukhina, I. V. Tropin, R. V. Kononenko, K. S. Burdin; UDC 502.31:581.51]

[Abstract] Study of the ecological and physiological patterns of the concentration of trace-element metals by marine macroalgae is timely in view of the growing anthropogenic pollution of the seas and coastal waters.

Analysis of the trace-element composition of various-aged sectors of highly differentiated thallomes of fucoids makes it possible to estimate the average level of metal content in a medium over a specific period of time. The researchers here chose to study the nature of the distribution of heavy metals—Cu, Zn, Mn, Cd, Ni, and Pb—in young (10-12 days) and mature (35-40 days) phylloids of *Sargassum pallidum* and in isolated biochemical tissue fractions. It was found that distribution in the basic biochemical fractions differed according to phylloid age, regardless of metal content in the medium. The differences may be associated with the age variation of the percentage of organic compounds in a unit of biomass, as well as with the variation in physiological status of tissue. The researchers do note that when the metal concentration in the medium is raised (0.3 mg/l), the metals are accumulated more intensely by the mature phylloids. Figures 1, references 5: 4 Russian, 1 Western.

**Fungi *Coriolus versicolor* Fr. (Quel.) 77 and *Kuehneromyces mutabilis* Sing. Et. Smith. 95—Efficient Destroyers of Alkaline Lignin**

937C0135C Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 4, Oct-Dec 91 [manuscript submitted 3 Apr 91] pp 61-65

[Article by I. A. Reshetnikova, V. V. Yelkin, T. M. Trifonova; UDC 547.992.3:579.222.2]

[Abstract] Properly resolving questions associated with the biodegradation of lignin is important in that it can help to protect the environment against high-level pollution by the phenols of the paper-pulp industry and the hydrolysis industry. It also opens the possibility of using lignin as a renewable resource for the production of organic- and microbial-synthesis products and may make possible the use of biolignolytic systems for bleaching pulp, for controlling environmental pollution caused by chemical wastes, and for purifying pulp-paper waste water. The researchers here study the ability of various xylophagous fungi to degrade a lignin in which there was no absorption maximum at  $\lambda$  280 nm. They find that the fungi *C. versicolor* strain 77 and *K. mutabilis* strain 95 have enzyme systems with lignolytic activity. Figures 2, references 20: 7 Russian, 13 Western.



# Infection Morbidity in USSR in 1990

937C0124A Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 12, Dec 91 (manuscript received 05 Jun 91) pp 20-22

[Article by M. I. Narkevich and G. G. Onishchenko, Chief Epidemiological Directorate, USSR Ministry of Health, Moscow; UDC 616.9:313.13(47+57)“1990”]

[Text] An alarming epidemiological situation is unfolding in the country. In 1990 alone 67.99 million cases of infectious diseases were reported and more than 50,000 people died, with an economic loss of 9.4 billion rubles (Table 1).

**Table 1. Infectious Diseases in the USSR in 1990 Compared With 1989**

Nosological Forms	Total Number of Diseases		Number of Cases per 100,000 Persons	
	1989	1990*	1989	1990*
Typhoid Fever	6,127	5,892	2.14	2.04
Paratyphoid A, B, C	3,317	2,736	1.16	0.95
Salmonellosis Infections	156,972	160,544	54.95	55.85
Total Acute Intestinal Infections	1,462,979	1,277,782	512.16	444.53
Including Bacterial Dysentery	391,545	381,453	137.07	97.91
Tularemia	158	202	0.05	0.07
Anthrax	174	232	0.06	0.08
Brucellosis, new cases	5,302	5,311	1.86	1.84
Diphtheria	852	1,431	0.29	0.49
Pertussis	37,540	33,589	13.14	11.68
Meningococcal Infection	12,358	10,939	4.32	3.80
Tetanus	213	243	0.07	0.08
Poliomyelitis	90	310	0.03	0.10
Measles	51,836	46,341	18.39	16.12
Tick-Borne Encephalitis	3,816	5,610	1.33	1.95
Hemorrhagic Fevers	6,591	2,814	2.30	0.97
Viral Hepatitis Infections	908,127	913,381	317.94	317.75
Hepatitis A	—	799,112	—	278.00
Hepatitis B	—	110,970	—	38.60
Ornithosis	—	106	—	0.03
Infectious Mononucleosis	—	5,561	—	1.93
Ricketts	1,826	2,254	0.63	0.78
Including Epidemic				
Exanthematous Typhus	35	24	0.01	—
Malaria	1,372	570	0.48	0.19
Teptospirosis	2,504	1,979	0.87	0.68
Acute Upper Respiratory Tract Infections	59,610,990	55,531,380	20,863.63	19,319.08
Influenza	8,765,207	9,600,403	3,068.52	3,339.94
Syphilis	—	13,636	—	4.74
Gonorrhea, Acute and Chronic	—	267,291	—	92.98
Scabies	—	82,805	—	28.80

\*Data for 1990 are preliminary, calculated using the 85-month form (Form 1 as of 01 Jan 92).

Increases in morbidity in 1990 were noted in salmonellosis, anthrax, and influenza.

More than 160,000 persons were affected by salmonellosis, and the epidemiological situation was aggravated in eight republics. Particularly significant growth has been noted in Byelorussian SSR by 82 percent, the Estonian Republic by 29 percent, and Kazakh SSR by 27 percent.

The morbidity index with viral hepatitis infections is 317.7 cases per 100,000, and the total number of victims was 913,400. Morbidity increased in the Ukraine (34

percent), RSFSR (18 percent), and Kazakh SSR and the Republic of Georgia. In spite of a sustained drop, the viral hepatitis morbidity level exceeds the union average by 2.7 times in the Republic of Uzbekistan, by 2 times in the Republic of Kyrgyzstan, and by 1.7 times in the Republic of Tadzhikistan.

A poor situation for acute intestinal infection morbidity has developed, with 1,010.2 cases per 100,000 in Tadzhikistan, 639.9 in Uzbekistan, 555.4 in Turkmen SSR, 543.4 in Kyrgyzstan, and 510.1 in the Republic of Moldova. Table 2 shows the specific weight of infection outbreaks.

**Outbreaks of Acute Intestinal Infections Recorded in 1990 by Union Republics**

Republic	Number of Outbreaks/Victims	Means of Transmission			Preschools	Pioneer Camps, Work and Rest Camps	Occupational and Technical Academies	Schools and Boarding Schools	Unorganized Public Groups	Employees at Industrial Enterprises	Other Organized Public Groups
		Water	Food	Milk							
RSFSR	16/5,451	2/2,208	10/496	4/2,747	1/57	4/141	1/43	4/245	6/4,955	4/337	13/253
Moldova	4,188	—	4/188	—	1/46	1/55	—	—	2/87	—	—
Ukraine	1/25	—	1/25	—	—	1/25	—	—	—	—	—
Latvia	3/5,451	—	2/66	1/5,385	—	1/29	1/37	—	1/5,827	—	—
Kazakhstan	1/821	—	—	1/821	—	—	—	—	1/821	—	—
Total...	25/11,936	2/2,208	17/775	6/8,953	2/103	7/260	2/80	4/245	10/11,690	—	—

The intensity of acute intestinal infection outbreaks has increased: 75 major influenza diseases and salmonellosis diseases were recorded (Table 3).

**Outbreaks of Acute Intestinal Infections Recorded in the USSR for 1986-1990**

Year	Number of Outbreaks/Victims	Means of Transmission			Preschools	Pioneer Camps, Work and Rest Camps	Occupational and Technical Academies	Schools and Boarding Schools	Unorganized Public Groups	Employees at Industrial Enterprises	Other Organized Public Groups
		Water	Food	Milk							
1986	97/13,222	15/1,405	50/2,808	19/8,756	29/1,009	11/726	3/182	13/922	29/9,751	4/337	13/253
											daily contact
1987	105/14,550	14/2,281	69/3,880	17/8,144	17/1,111	18/941	3/123	12/778	39/10,712	3/210	5/245 SCO
1988	74/9,347	7/781	53/3,430	14/5,136	2,066	807	71	674	5,140	118	242 SCO
1989	61/9,693	10/1,256	37/2,623	14/5,814	17/2,514	9/412	2/77	7/1,076	23/5,507	1/50	
1990	25/11,936	2/2,208	17/775	6/9,395	2/103	7/260	2/80	4/245	10/11,690	—	

\* Student construction group

The greatest number of outbreaks occurred in the RSFSR (38), Ukraine (10), and Kazakh SSR (11). The largest outbreak in the past 10 years (5,385 victims) was recorded in a number of regions in Latvia due to the consumption of products from the Yelgavskiy Dairy contaminated with the dysentery etiological agent.

In November 1990, 1,768 persons in Langeepas, Tyumen Oblast, became ill with dysentery. The cause of the outbreak was drinking water contaminated as a result of an accident at a sewage pump station.

The number of salmonellosis outbreaks is increasing. Outbreaks of typhoid are still recorded (Table 4).

**Table 4. Outbreaks of Typhoid Fever and Other Salmonellosis Infections Recorded in the USSR for 1988-1990**

Union Republic	Salmonellosis			Typhoid Fever		
	1990	1989	1988	1990	1989	1988
USSR	53/6,016	70/6,872	45/4,048	4/183	8/350	7/276
RSFSR	22/2,909	47/4,876	24/2,424	2/127	2/59	2/60
Ukraine	9/1,274	6/914	3/214	—	—	—
Byelorussian SSR	2/197	1/25	—	—	—	1/23
Republic of Uzbekistan	—	1/16	2/18	—	5/276	2/98
Kazakh SSR	10/855	—	2/114	—	—	—
Republic of Georgia	—	—	—	—	1/15	1/81
Republic of Azerbaijan	—	—	—	—	—	—
Republic of Lithuania	—	—	—	—	—	—
SSR of Moldova	6/378	10/734	12/944	—	—	—
Republic of Latvia	—	3/218	—	—	—	—
Republic of Kyrgyzstan	1/100	—	—	2/56	—	1/14
Republic of Tadzhikistan	1/74	—	2/334	—	—	—
Republic of Armenia	1/120	—	—	—	—	—
Turkmen SSR	1/110	—	—	—	—	—
Republic of Estonia	—	2/90	—	—	—	—

Note. The numerator indicates the number of outbreaks; the denominator indicates the number of cases per outbreak.

Cholera morbidity increased. In July of last year 49 cases of cholera and 20 carriers of this infection were recorded among those vacationing and working at the Rodnik campground in Stavropol. Cholera and carriage of the cholera vibrio was diagnosed in 20 Soviet tourists returning from Calcutta to Moscow. Four persons became ill with cholera in August 1990 in Rostov and the adjacent Azov Rayon.

This is the result of grave flaws in the work of Soviet and economic agencies at the sites for ensuring the sanitary and epidemiological welfare of the public and their weak insistence of the factory directors and organizations and thus suggests the need for a complex approach to controlling infections.

Particularly unacceptable is the increase in diphtheria and poliomyelitis morbidity, infections for which there are effective prophylactic measures.

In the Azerbaijan Republic 164 children fell victim to poliomyelitis, which was 53 percent of all victims in the country in 1990.

Morbidity with this infection in 1990 was aggravated in Turkmen SSR (39 cases) and the Republic of Uzbekistan (37 cases).

Investigation of the outbreak in the Azerbaijan Republic established that 78 percent of the affected children were either not immunized or they lacked information about the vaccinations.

Unfortunately, the low level of the scope with immunizations has become a widespread problem. Vaccination

last year against diphtheria encompassed only 79 percent of the children under 1 year of age in the country, 61.6 percent of the Republic of Kyrgyzstan, and 67.7 percent in the Republic of Georgia.

Only 74.6 percent of children in the country were vaccinated against poliomyelitis at the scheduled periods. In the Russian Federation and the Republic of Uzbekistan, this index was 68.6 and 61.2 percent, respectively.

The unsatisfactory organization of vaccinations resulted in a diphtheria outbreak in Moscow in 1990, where 688 persons were infected. The reasons for this situation are in part associated with the widespread campaign against immunization that began two years ago in the press, which has sharply affected the scope with vaccinations due to the increasing number of refusals.

There are reasons lying outside the competence of the local agencies and establishments. They are the aggravated sociopolitical situation in a number of regions of the Caucasus, Central Asia, and the Russian Federation.

Since 1988 an unprecedented situation has developed in the country, when immunological productions of the most widespread vaccines, measles and BTsZh [as published], closed due to poor quality.

In order to solve these problems, as well as fulfill the commitments made by our country to the world community to eradicate a number of infectious diseases and remove disruptions in the supply and creation of new immunobiological preparations, it was necessary to

develop a government-union-republic program for infection prophylaxis to be controlled with vaccines, "Immunoprophylaxis". We set about such a program.

Hepatitis B morbidity increased and was 38.6 cases per 100,000 persons in 1990, or 110,000 cases.

The specific weight of the republics in Central Asia in morbidity in the country was 42.5 percent. Moreover, in the Republic of Uzbekistan the morbidity level exceeds the average for the country by two-fold.

Hepatitis B is one of the most acute problems of national public health. More than 5,000 persons die of the disease in the country each year. The primary reasons for the increasing number of victims of this infection are blood transfusion and medical intervention (in addition to sexual means of transmission).

Immunization is an effective means of specific prophylaxis for this form of the disease. The vaccines available in the practice of world public health have had good results, making it possible to eradicate hepatitis B in the near future.

The USSR Ministry of Health is taking all the measures necessary to accelerate the development of Soviet vaccines or purchase the foreign technologies; however, this entails a great deal of hard-currency investment.

In 1990, 82,800 cases of scabies were recorded, a 13 percent increase over 1989 figures. There were 578,000 cases of pediculosis.

Five cases of plague were recorded, two of which were fatal.

In order to stabilize the increase in preventable infection, conditions need to be established for the more effective prophylaxis of intestinal infections for preventing outbreaks of these diseases. The following measures need to be implemented:

Activate the work of the emergency anti-epidemic commission of the union republics, review the current situation, establish plans for additional, urgent measures for preparing enterprises and installations of water and sewage management, food and dairy industry, public eating and trade enterprises, pioneer camps and rural preschools for working in the spring and summer. Demand that the directors of these establishments carry out urgent measures for the prophylaxis of infectious diseases and preventing the development of outbreaks of acute infections.

Consider that in the current tense epidemiological situation, which is due to a decrease in the standard of living of the people and imbalance in national economy connections, which ultimately results in deterioration in meeting the primary needs of the public, effective implementation of prophylactic and anti-epidemic measures is possible only when based on the coordinated efforts of all concerned departments and organizations.

It is necessary to take urgent measures for stabilizing the supply of medical establishments in the country with immunobiological preparations for the prophylaxis, diagnosis, and treatment of infectious diseases to meet the requirements of the World Health Organization.

With the objective of prophylaxis of the most widespread infectious diseases, the USSR Ministry of Health needs to develop with the involvement of concerned ministries, departments, and organizations a union republic program "Immunoprophylaxis", to include:

- a unified system of production and supply with medical immunobiological preparations for the prophylaxis, diagnosis, and treatment of the most widespread infectious diseases, financial and technical support for the production of immunobiological preparations, capital construction, and the purchase and development of the necessary technological equipment and raw material supply; fundamental medical and theoretical research on the creation of new and improvement of existing vaccines and diagnostics;
- development of organizational aspects of the strategy and tactics for immunoprophylaxis in the public health establishments and regional calendars for vaccinations;
- creation of conditions for studying individual immunity and adjusting it with respect to the results obtained;
- support for the legal basis of immunization, education, and medical education of the public.

Prepare and implement during 1991 a regional program for prophylaxis and decreasing morbidity and fatality from the most widespread acute infectious diseases in Central Asia.

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### Description of Plague Epidemics in USSR for 1920-1989

937C0124B Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 12, Dec 91 (manuscript received 30 Oct 90) pp 31-33

[Article by M. I. Narkevich, G. G. Onishchenko, A. V. Naumov, Yu. M. Fedorov, A. M. Kokushkin, A. I. Kologorov, and A. Z. Berezhnov, Chief Epidemiological Directorate, USSR Ministry of Health, Moscow; All-Union Anti-Plague Scientific Research Institute, USSR Ministry of Health, Saratov; UDC 616.98:579.842.23]-036.22.(47+57)"1920-1989"]

[Text] Natural plague breeding grounds cover 216 million hectares, or 9.6 percent of the USSR. At present, the borders of 16 autonomous breeding grounds located within the regions of the Caucasus, norther Caspian Sea area, Central Asia, and Siberia have been determined, generally within the administrative areas of several union republics (Fig. 1). In an enzootic area the plague is expressed in the form of epizootics among the carriers of the infection (fleas and ticks), as well as camel diseases.

Human morbidity in the USSR, according to numerous published sources, was considerable until the 1930's. Data on plague epidemics in the later periods are lacking.

The objective of this work is to analyze plague morbidity in the country for 1920 through 1989 using archive data from the Laboratory of Plague and Cholera Epidemiology at the All-Union Anti-Plague Scientific Research Institute "Mikrob".

During this period plague disease was recorded and confirmed in 3,639 persons, of which 2,660 (73 percent) died.

The highest epidemic activity was observed in the Central Asian desert breeding grounds, where there were 1,826 cases recorded in 1920, half of the total number of cases in the country. Sporadic cases of human infection are still recorded here.

In the RSFSR, where 1,302 cases have been recorded (35.8 percent of the total number), a group of natural breeding grounds in the northern Caspian Sea area presents the most serious epidemic hazard. The last case of plague disease here occurred in 1979.

Natural breeding grounds in the Caucasus, where there have been 291 human cases of plague disease (7.9 percent) during the period in question, present a somewhat lesser threat due to the preferential circulation of the slightly virulent "field" strains. The last case here was identified in 1975.

Slight epidemic activity has been noted in the mountain regions of Central Asia, where 112 human cases (3.1 percent) have been recorded, and in a group of Siberian breeding grounds. The last cases identified there were in 1981 and 1960, respectively.

The greatest number of plague cases during these years were in Kazakhstan (50.2 percent of all cases), the RSFSR (35.8 percent), and Azerbaijan (6.1 percent). In the remaining republics (Kyrgyzstan, Georgia, Turkmenistan, Uzbekistan, and Armenia) morbidity was much lower (0.03 to 3.1 percent of all cases in the country).

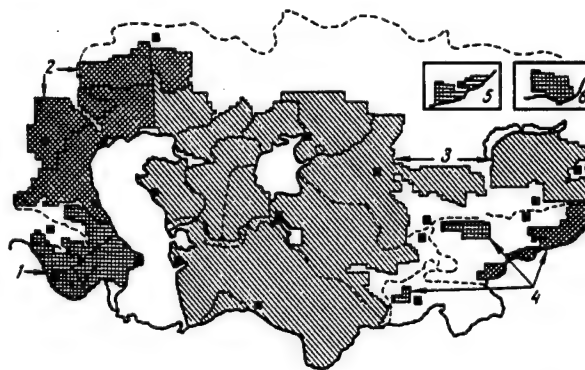


Fig. 1. Natural plague breeding grounds in the USSR.

Key: 1. Breeding grounds in the Caucasus; 2. Breeding grounds in the northern Caspian Sea area; 3. Central Asian breeding grounds; 4. Mountain breeding grounds in Central Asia; 5. Breeding grounds in Tuva and Altay; 6. Baikal breeding grounds.

An analysis of plague morbidity dynamics in the USSR during the past 70 years (Table 1) shows that four periods can be isolated which characterize the varying intensity of the epidemic of infection: 1920-1929, when thousands of plague cases were recorded; 1930-1949, when there were hundreds of cases; 1950-1969, when there were dozens of cases; and 1970-1989, when there have only been sporadic cases of human infection.

Table 1. The Number of Human Victims and Dead From the Plague Within the USSR for 1920-1989 (Current Administrative Division)

Territory	1920-1929	1930-1939	1940-1949	1950-1959	1960-1969	1970-1979	1980-1989	Total
RSFSR	1,067/673	227/193	3/2	1/1	3/—	1/1	—	1,302/870
Kazakhstan	1,269/1,237	147/97	329/56	22/9	43/13	11/5	5/1	1,826/1,418
Uzbekistan	—	—	46/3	—	2/2	1/1	2/—	51/6
Kyrgyzstan	79/71	—	13/10	2/—	15/5	—	3/—	112/86
Turkmenistan	—	—	3/1	51/5	1/1	—	—	55/7
Armenia	—	—	—	—	—	1/1	—	1/1
Azerbaijan	—	206/203	15/—	—	1/1	—	—	222/204
Georgia	70/68	—	—	—	—	—	—	70/68
Total	2,485/2,049	580/493	409/72	76/15	65/22	14/8	10/1	3,639/2,660

Note: Numerator indicates number of victims, denominator indicates number of dead.

As a whole the human morbidity level for 1980-1989 has decreased by 220 times when compared with 1920-1929 and by 39 times when compared with 1940-1949.

The high level of morbidity for 1920-1949 is attributed to the advent of intensive plague outbreaks on significant areas of southeastern Russia, the Volga-Ural Interfluvium,

Central Asia, and the Baikal area. In connection with the poor development of anti-plague establishments in the country and the tardiness of anti-epidemic measures, we often observed a transition of the disease to the pulmonary form with the subsequent anthroponotic spread of the infection. Examples of pulmonary plague outbreaks occurred in Primorye (1920-1921), the northern Caucasus (1933), and Avani (1947), during which there were hundreds of cases.

During 1950-1969 along with plague outbreaks (from 9 to 47 persons) in the desert breeding grounds of the Central Asian republics, there were sporadic cases in the natural mountain breeding grounds.

Over the past 20 years (1970-1989) plague disease has been recorded only during the past 10 years. There was one plague outbreak: five persons became infected when they slaughtered a sick camel. The rest of the cases were sporadic. Early detection and isolation of victims and effective treatment prevented the transition of the disease to the pulmonary form: only the bubonic and septic forms of plague were recorded.

Retrospective analysis of the epidemic display of different plague breeding grounds since 1940 shows that human infection most often occurs as a result of being bitten by an infected flea, and more rarely upon direct contact with sick camels. Infection was even more rarely contracted from contact with infected rodents (Table 2).

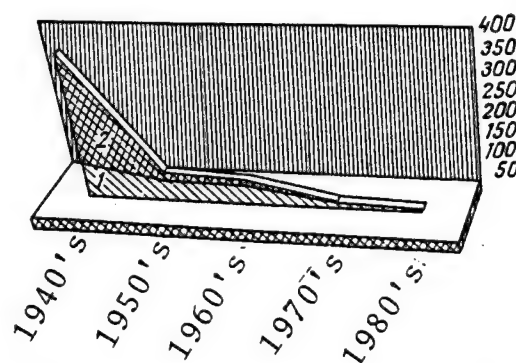
**Table 2. Means of Human Infection in Natural Plague Breeding Grounds**

Years	Infected	Transmissible Period	Infection by Contact	
			With Wild Rodents	With Camels
1940-1949	87	53	4	30
1950-1959	49	28	2	19
1960-1969	45	12	8	25
1970-1979	14	7	2	5
1980-1989	8	7	1	—
Total	203	107	17	79
	(100%)	(52.7%)	(8.4%)	(38.9%)

Representatives of the following occupational groups were infected by plague in natural breeding grounds: shepherds and members of their families (69.9 percent), workers in enzootic areas (9.9 percent), hunters (6.5 percent), medical personnel (5.9 percent), lengthmen (3.4 percent), agricultural workers (3.4 percent), semi-diesel engine workers (0.5 percent), and servicemen (0.5 percent). Bubonic plague was found in 82.7 percent of the victims infected in nature, the septic form was found in 16.7 percent, and the pulmonary form was found in 0.6 percent. Plague spread from person to person in 63.5 percent of cases transmissibly, in 34.9 percent by airborne droplets, and in 1.6 percent of cases by contact.

The steady decrease in human morbidity has been attained primarily by preventing transmission of the etiological agent from person to person (Fig. 2). Thus, whereas the proportion of individuals infected by contact with an affected individual was 75 percent in the 1940s, in the 1950s it decreased to 30 percent, and in the 1960s to 18 percent. To date, cases of plague infection from affected individuals have not been recorded.

At present, periodic epizootological screening is performed at all 16 known natural breeding grounds for plague. During the past five decades 29,424,680 rodents were trapped and subjected to bacteriological screening (by decades: 10.8, 15.9, 21.5, 27.8, and 24.4 percent) and 197,452,019 ectoparasites were trapped and screened (respectively 6.4, 13.7, 23.4, 31.5, and 25 percent). In addition, 102,095 *Yersinia pestis* cultures were isolated



**Fig. 2. Number of persons infected with plague in natural breeding grounds and from another person during the period 1940-1989.**

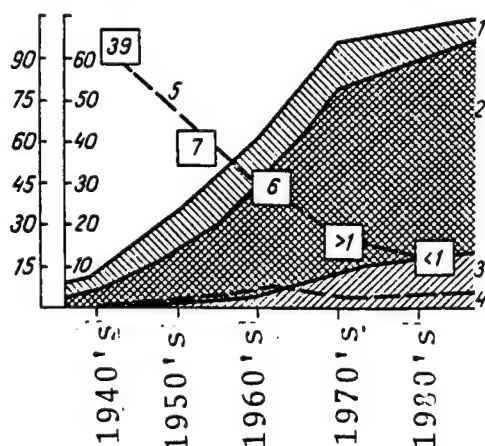
Key: 1. Proportion infected from animals; 2. Proportion infected from another person.

with the following distribution by decades: 3.4, 9.5, 28.5, 35.5, and 23 percent. Beginning in the 1960's serological screenings detected 106,349 animals with specific antibodies to the plague etiological agent.

Against a background of increasing volumes of epizootological screenings and prophylactic measures in the breeding grounds, the epizootic activity of natural plague breeding grounds (according to indexes of cultures isolated and the area of the epizootics) increased from 0.09



percent of the enzootic area in the 1940's to 2.3 percent in the 1950's and in the future will be 1.5-3 percent of the natural breeding ground area annually (Fig. 3). At the same time the prompt identification of epizootics, increasing the volumes of epizootological screening, and respectively goal-oriented prophylactic measures decreased the risk of human infection in nature and the likelihood of the anthroponotic spread of plague.



**Fig. 3. Dynamics of prophylactic measures performed in natural plague breeding grounds.** The X-axis shows the years, the Y-axis shows the number of analyses (in millions) from the left, and the percentage of territory of natural breeding grounds from the right.

Key: 1. analyses performed (in millions); 2. territory screened, in percentage of total area of the natural plague breeding grounds in the USSR; 3. area of conducted prophylactic measures in percent from the total area of natural sources of plague in the USSR; 4. area of epizootics in percent of total area of the natural plague breeding grounds in the USSR; 5. number of plague victims per year (the average annual number of victims by decade are shown in the squares).

Thus, the effective work of the anti-plague establishments of the country has ensured epidemiological well-being where the epizootic activity of the natural plague breeding grounds has not decreased. In addition, the migration of the public into the natural breeding grounds and from them to non-enzootic areas in recent years has considerably increased. Agricultural, construction, and

industrial development of areas enzootic for plague has increased. To date 99 million hectares, or 45.8 percent of these areas have been subjected to the anthropogenic factor, where there are more than 30 installations that have been constructed that are of national significance. All of this increases the level of contacts between the public and the natural breeding grounds.

Living in the enzootic area are 41.5 million persons, of which 3.1 million were subjected to direct risk of plague infection in 1989. Of these, 2.6 million of the permanent population had direct contact with natural breeding grounds. The contingents at greatest risk are stock breeders and members of their families, hunters and professional fishermen, feed grain manufacturers, veterinary personnel, agronomists, machinery maintenance engineers, automobile and railroad repairmen, and telecommunication station workers. It should be noted that the social and living conditions of the above listed contingents remain primitive and have been virtually unchanged over the past decades.

A temporary population of 469,000 persons is also at high risk of infection in the enzootic territory. In this group are agricultural workers (shepherds and their families who are involved in stock breeding, city dwellers employed for the harvest, etc.), shift workers, geologists, archaeologists, tourists, bus drivers, etc. The number of tourists (76,000) and shift workers (47,000) is particularly high. These groups of the temporary population are endangered by their migration into non-enzootic areas of the USSR and abroad. Following infection in a natural breeding ground, with the capabilities of modern transportation a person could reach any point on the face of the earth within the incubation period.

In conclusion, it should be stated that the epizootic activity of natural plague breeding grounds in the USSR remains high; therefore, there is still the risk of human infection with plague in natural breeding grounds. As a rule, natural plague breeding grounds are located in several union republics. The Central Asian desert breeding ground and the group of Caspian natural breeding grounds present the greatest epidemiological hazard. The goal-oriented work of anti-plague establishments, under conditions of continuing activity of the natural breeding grounds, will ensure epidemic well-being with respect to the plague.

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**Preparation of Highly Purified Recombinant  $\beta$ -Galactosidase- $\beta$ -Interferon Conjugate for Enzyme Immunoassay**

937C0078B Moscow DOKLADY AKADEMII NAUK  
in Russian Vol 324 No 5, Jun 92 (manuscript received  
20 Mar 92) pp 1121-1124

[Article by A.N. Markaryan, Yu.A. Motorin, B.V. Perelman, N.V. Gorokhovets, S.V. Mashko and A.M. Yegorov, Institute of Biochemistry imeni A.N. Bakh, Russian Acad. Sci., Moscow; Institute of Genetics and Selection of Industrial Microorganisms, Moscow; Moscow State University imeni M.V. Lomonosov; UDC 577.154.25]

[Abstract] Cursory details are provided on the construction of plasmid pUR1 bearing a hybrid gene encoding *E. coli*  $\beta$ -galactosidase and human  $\beta$ -interferon; expression of the hybrid protein was placed under the control of the lac-promoter. Transformation of *E. coli* TG1 cells with pUR1 yielded the 136 kD hybrid protein which exhibited  $\beta$ -galactosidase activity (550 U/mg) and bound monoclonal antibodies against  $\beta$ -interferon. Sensitivity of conjugate-based fluorometric and photometric versions of competitive enzyme immunoassay for  $\beta$ -interferon was on the order of 5-10  $\mu$ g/ml. However, further gains in sensitivity can be anticipated by the use of higher affinity antibodies. Figures 2; references 11: 3 Russian, 8 Western.

**Immunopeptide Priming of Macrophages**

937C0079A Moscow DOKLADY AKADEMII NAUK  
in Russian Vol 323 No 4, Apr 92 (manuscript received  
10 Jan 92) pp 354-357

[Article by L.V. Kovalchuk, R.Ye. Titovets, L.V. Gankovskaya, N.E. Aptsiauri and V.A. Izvekova, Moscow State Medical University imeni N.I. Pirogov; UDC 576.8.097.3:616.153-0081]

[Abstract] An analysis as conducted on the relative efficiency of recombinant TNF- $\alpha$  and IL-2, and natural immunopeptides (NI) from a culture of porcine monocytes, in the priming of macrophages derived from 18-20 g C57BL/6 (H-2<sup>B</sup> male mice. In terms of priming efficiency the factors under consideration ranked as follows: IL-2 < TNF- $\alpha$  < IN, with corresponding indexes of stimulation of 1.6 < 1.8 < 3.7. The greater efficiency of IN was attributed to its composition which includes IL-1, IL-2, TNF- $\alpha$ , interferon- $\gamma$ , and a number of other bioactive factors which render NI effective at low concentrations (10-20  $\mu$ g/ml). Primed macrophages responded both with increased levels of active oxygen as well as with enhanced production of arachidonic acid. In addition, macrophages pretreated with NI for 24 h were extremely effective in killing melanoma B16 cells. Figures 3; tables 1; references 7: 2 Russian, 5 Western.

**Natural Gas-Induced Pathology in Pulmonary Microvasculature: Health Risk Assessment in Astrakhan Region**

937C0160A St. Petersburg MORFOLOGIYA in Russian  
Vol 102 No 2, Feb 92 (manuscript received 28 Jun 91)  
pp 64-70

[Article by R.I. Asfandiyarov, A.Ye. Lazko, M.V. Lazko and S.B. Motalin, Chair of Human Anatomy, Astrakhan Medical Institute imeni A.V. Lunacharskiy; Cost Accounting Center for Biomedical Research, Union of Scientific Medical Societies of the Astrakhan Oblast; UDC 611.16:616.24:613.632.4:599.323.4]

[Abstract] Histopathologic studies were conducted on pulmonary microcirculatory system in 190-230 g outbred male rats to assess the adverse effects of natural gas. Examinations were performed after 5, 15, 30 or 60 min of exposure to natural gas prevalent in the Astrakhan region, containing 730 mg/m<sup>3</sup> of hydrogen sulfide. The results showed that the extent of microvascular and alveolar damage was directly related to the duration of exposure, with initially reversible changes becoming irreversible. These included increasing vascular permeability, exudation, rouleau formation, thickening of the capillary walls, endothelial damage, stasis, erythrocyte degradation and destruction of alveoli. The observations have obvious implications for human health that need to be more closely scrutinized. References 10: 8 Russian, 2 Western.

### Histological Description of Eye Structures After Various Sections of the Lens Are Exposed to Yag Laser in Experiment

937C0116A Moscow VESTNIK OFTALMOLOGII in Russian Vol 108 No 3, May-Jun 92 [manuscript submitted 27 Jun 91] pp 10-14

[Article by Khasan Abdul Karim, N. G. Mamedov, A. V. Kaplina, and D. O. Kolesnikov, Department of Eye Diseases, Treatment Faculty, Second Moscow Medical Institute imeni N. I. Pirogov; UDC 617.741-085.849.19-036.8-07:617.7-076]

[Abstract] The researchers here conducted a series of experimental studies on 79 eyes of chinchilla rabbits that weighed 3.5-4 kg each. After the eyes of the rabbits were exposed to the yag laser, the eyes were enucleated after the following periods of time: 1-24 hours and 7-10 days. The enucleated eyes were then subjected to the standard histological processing. Yag-laser capsular puncture and fragmentation of the intracapsular structures were performed with an Opton Visulas XAb laser unit. A total of 31 rabbit eyes were subjected to yag-laser capsular puncture—16 of them at 3 mJ, and 15 at 5 mJ. Fragmentation of the intracapsular structures was performed on 23 rabbit eyes—on 13 at 3 mJ, and on 10 at 5 mJ. A total of 25 rabbit eyes were subjected to a combined procedure—successive intracapsular fragmentation and capsular puncture—with 12 of the eyes subjected to 3 mJ and 13, to 5 mJ. In all cases, the yag-laser puncture was performed in the following manner: the focal plane of the laser radiation was strictly on the surface of the capsule (diameter 30 fm). A total of 8-12 punctures were made in the capsule, with the punctures located in a circle with a diameter of 5-6 mm. The energy level was 3-5 mJ. In the yag-laser fragmentation of the intracapsular sections of the lens, the focal plane of the laser radiation was in the cortical layers of the eyes. The procedure entailed concentrating 65-70 pulses of radiation in a circle with a radius of 4-5 mm. When the laser's probing was deeper than the cortical layer, the radiation was concentrated in a much smaller circle, which had a radius of around 2-3 mm, or it was applied along lines that were perpendicular to each other and that intersected at the center of the lens. A third series of studies were performed after the combined procedure on the 25 eyes. The researchers observed that the irradiation produced destructive changes such as edema of the epithelium of the crystalline capsule, splitting of the epithelial layer, sagging and bulging of the anterior crystalline capsule, punctures, multilayer proliferation of the epithelium in the focal and perifocal areas, and fiber splitting and fragmentation. The nature and extent of the pathomorphology were a direct function of level of energy and time of examination after exposure to the laser. The primary destructive effects of the fragmentation were in the focal area. The range of 3-5 mJ proved to be the most effect energy range, and the combined procedure accelerated and intensified the swelling and fragmentation of the cortical layers of the lens, precluding surgical dissection of the anterior crystalline capsule. Figures 6, references 9: 5 Russian, 4 Western.

### Thymoptin, T-Activin and Decaris Immunotherapy in Endogenous Uveitis

937C0144A Odessa OFTALMOLOGICHESKIY ZHURNAL in Russian No 1, Jan-Feb 92 (manuscript received 20 May 91) pp 1-5

[Article by M.A. Penkov, prof., S.F. Zubarev, doc., N.M. Avrushchenko, cand. med. sci., and N.V. Panchenko, fellow, Chair of Eye Diseases, Kharkov Medical Institute; UDC 617.721-002.6-085:615.37]

[Abstract] Therapeutic trials were conducted with thymoptin, T-activin and Decaris in the management of patients with "endogenous" uveitis and abnormal immunologic workups. The patient cohort consisted of 144 males and females ranging in age from 13 to 79 years; uveitis was describe as severe in 134 of the patients and as light-moderate in 10. Thymoptin, a preparation containing  $\alpha$ -thymosin, was administered subcutaneously q. 3-4 days in a dose of 80  $\mu$ g for a cumulative dose of 262  $\mu$ g. The cumulative T-activin dose was 184  $\mu$ g (20-40  $\mu$ g every other day, s.c.), and the total Dekaris dosage came to 1100 mg (100-150 mg/day for 2-3 days/week for 3-4 weeks, or 100-150 mg/day for 7-8 days). After the course of therapy significant ( $p < 0.001$ ) elevations were noted in T-lymphocytes and T-helpers. Patients on Dekaris also showed a similar increase in T-suppressor counts. B-lymphocytes and IgA, IgM and IgG levels were not affected. In addition to improvements in cellular immunity, thymoptin and T-activin were effective in reducing the time required for control of ocular inflammation by 30-35 percent in comparison with patients on Dekaris. Full clinical details on the efficacy of thymoptin and T-activin shall be published separately. Tables 4; references 9: 8 Russian, 1 Western.

### Bioregulators and Phagocytosis

937C0144B Odessa OFTALMOLOGICHESKIY ZHURNAL in Russian No 1, Jan-Feb 92 (manuscript received 18 Sep 91) pp 26-31

[Article by T.V. Degtyarenko, cand. med. sci., Odessa Order of the Red Banner of Labor Scientific Research Institute of Eye Diseases and Tissue Therapy imeni acad. V.P. Filatov; UDC 616-097-092.18:615.322]

[Abstract] A series of bioregulators representing a variety of sources were tested for the effects on peritoneal macrophages of C57B1/6 mice with congenital T-cell immunodeficiency. The trials included a novel peloid designated PMM (plasma membrane activator) developed at the Odessa Medical Institute's Biochemistry-Virology Laboratory, as well as placental extracts, aloe vera preparations, torfot [sic], and FiBS. Phagocytic function was analyzed in terms of hydrogen peroxide and active oxygen production and metabolic bursts as evident in chemiluminescence. The agents were administered either as a single intraperitoneal injection or as a series of subcutaneous injections. This approach was shown to be effective in determining the degree to which metabolic activity of the macrophages was stimulated

and of their antigen-processing potential. The effectiveness of PMM was especially encouraging in view of the peloid resources of the Odessa region. Figures 3; tables 1; references 6: Russian.

**Physicochemical Assessment of Ion Exchange Inserts in Alkali Eye Burns**

937C0144C Odessa *OFTALMOLOGICHESKIY ZHURNAL* in Russian No 1, Jan-Feb 92 (manuscript received 28 Jun 90) pp 44-46

[Article by Yu.F. Khatminskiy, prof., and G.G. Basova, cand. med. sci., Chair of Eye Diseases, Kemerovo Medical Institute; UDC 617.713-001.37:612.085.1-085]

[Abstract] Experimental therapeutic trials were performed with cation exchange resin KB-4—dispersed in a polyvinyl alcohol gel—in the management of alkali ocular burns. The experiments utilized 2.0-2.5 kg chinchilla rabbits, using 5 drops of 5 percent NaOH instilled on the cornea. The results showed that instillation of the gel had marked therapeutic effects due to restoration of normal acid-base balance as a result of removal of Na and Ca ions and reduction of edema. Within 10 min of gel application swelling was reduced approximately five-fold and excess sodium concentration two-fold. The efficacy of this form of therapy was attributed to the fact that the 0.7 g inserts have the capacity to neutralize 5.0-9.0 mg of NaOH on the corneal surface and absorb 0.8-1.2 mg of sodium. Tables 2; references 4: Russian.

**Cholera Phages From Open Water Bodies of Lake Issyk-Kul Basin and Their Taxonomy**

937C0123A Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 12, Dec 91 (manuscript received 19 Nov 90) pp 10-13

[Article by Yu. I. Arutyunov, L. D. Makedonova, S. R. Sayamov, R. A. Kazakbayeva, L. R. Tolmacheva, and L. V. Bezv, Rostov-on-the-Don Anti plague Scientific Research Institute; UDC 614.777:579.843.1/-074]

[Abstract] The objective of this investigation was to find phages in the Issyk-Kul Basin (Kyrgyzstan) that were active with respect to 01 and non-01 group vibrios, study the properties of the original phages, and determine their taxonomy. Water samples (3 liters every 10 days for 1.5 years) from Issyk-Kul were collected and examined for the presence of vibrio phages and vibrio-cholerae 01 and non-01 groups with the objective of identifying possible hosts. The specificity and range of action of the phages were studied on 1,487 strains of various members of the *Vibrionaceae* family. The results showed that both 01 and non-01 group cholera vibrios and cholera phages were found in open water bodies of the Lake Issyk-Kul Basin. Based on study of the specificity and range of action, as well as serological and morphological study, two isolated phages (119.60 and 133.60) can be classed as typical representatives of a new type of cholera phage which has no analogs in the presently accepted classification of *V. cholerae* phages. In conclusion, it is recommended that *Vibrio* genus phages be systematized within the framework of a unified classification of vibrio phages because of complexities arising in determining the specificity of cholera phages. Figures 1; tables 2; references 9: Russian.

**Pathogenesis of Q-Fever After Intratracheal Infection of Guinea Pigs**

937C0123B Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 12, Dec 91 (manuscript received 16 Oct 90) pp 48-51

[Article by T. A. Suvorova, V. A. Pshenichnov, and P. A. Grabarev, Microbiology Scientific Research Institute, USSR Ministry of Defense, Zagorsk; UDC 616.98:579.881.13]-092-092.9]

[Abstract] The dynamics of the accumulation and spread of *C. burnetti* strain ZhM, 3.9-4.4 lg ID<sub>50</sub>, in the blood and organs was investigated in guinea pigs (250-300 g) infected intratracheally and intraperitoneally (control) with a 20 percent suspension in a sucrose-agar-gelatin medium. The data revealed that *C. burnetti* was found in the lungs and spleen within 24 hours of infection, with generalization of the process occurring in the next 3-5 days. Comparison of the indexes of the infection process showed that with comparable infection doses, intratracheal infection is more pronounced than intraperitoneal infection. Since intratracheal infection is the closest to aerogenic infection, which is the most common route of

human infection under natural conditions, the data and route employed need to be considered in the experimental development of methods for preventing and treating pulmonary Q-fever. Tables 1; references 15: 13 Russian, 2 Western.

**Cytotoxic Properties of Recombinant Hybrid of A-Protein *Staphylococcus aureus* With Fragment of *Pseudomonas aeruginosa* Exotoxin A**

937C0142A Moscow *MOLEKULYARNAYA BIOLOGIYA* in Russian Vol 25 No 5, Sep-Oct 91 (manuscript submitted 30 Nov 90) pp 1188-1196

[Article by A. G. Tonevitskiy, V. A. Rakhmanova, A. Yu. Topygin, A. G. Zdanovskiy, G. V. Yershova, M. V. Zdanovskaya, N. M. Rutkevich, N. K. Yankovskiy, All-Union Cardiology Science Center, USSR Academy of Medical Sciences, Moscow; All-Union Scientific Research Institute of Genetics and Selection of Industrial Microorganisms, Moscow; UDC 57:083.3]

[Abstract] Combining the genes of two or more proteins to produce hybrid molecules holds a great deal of promise in biotechnology, and one of its applications is in the creation of targeted-action cytotoxic preparations. In previous work, this group of researchers selectively removed a population of cells by exposing them to specific antibodies that were combined with a toxin through chemical conjugation. In the work reported here, they used two models to study the properties of a chimeric protein they produced and the possibilities of its use as a targeted-action preparation. In the first model, the target cells were human Daudi B lymphoma cells expressing Ig on their surface. The hybrid toxin was delivered to the target with polyclonal antibodies to human Ig L-chains. A lysate of strain pAPA4 containing the hybrid molecule in a concentration of 10<sup>-8</sup> M inhibited protein synthesis by 13 percent, a figure that rose to 50 percent when the concentration was 10<sup>-7</sup> M. That is roughly equivalent to the cytotoxic activity recorded for isolated A subunits of ricin and the catalytic fragment of pseudomonas exotoxin and is below the activity of the native pseudomonas exotoxin by a factor of 10<sup>5</sup>. Thus, the gene-engineered pseudomonas exotoxin has virtually no toxic activity against the Daudi cells, probably because its structure has no toxin B fragment region to ensure binding with specific cell receptors. The cytotoxic activity of the hybrid toxin was also assessed for target cells consisting of human Jurkat T lymphoma cells, which were initially exposed to monoclonal antibodies to LT1 CD5-antigen, and then to polyclonal antibodies to mouse Ig and, after washing, the hybrid protein. The hybrid protein alone inhibited the inclusion of [<sup>14</sup>C]-leucine by 42 percent. Inhibition rose to 54 percent when the cells were incubated with antibodies and then with the toxin. Figures 5, references 19: 8 Russian, 11 Western.



**Expression of Human Tissue Plasminogen Activator With Recombinant Lines of Cells of Various Animals**

937C0142B Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
(manuscript submitted 14 Jan 91) pp 1226-1238

[Article by S. B. Aleshkov, M. B. Ustav, A. A. Bayev, Institute of Molecular Biology imeni V. A. Engelhardt, USSR Academy of Sciences, Moscow; Estonian Biocenter, Estonian Academy of Sciences, Tartu; UDC 57:085.23:577.214.625]

[Abstract] In the creation of recombinant lines of producer cells used in protein therapy, proper choice of cell line, i.e., host, is important. The existence of phylogenetic and intertissue differences in the mechanisms of processing and modification must be taken into consideration in the development of processes for producing fast-acting proteins introduced directly into the blood, such as tPA. The researchers here describe a set of recombinant lines of cells they produced that express human tPA. The cells were from various kinds of tissue from mice, rats, Chinese hamsters, and humans. Despite the species differences, the recombinant tPA they secreted exhibited no appreciable differences in the context of electrophoretic mobility or fibrinolytic activity. A modicum of heterogeneity of product in terms of molecular weight stems from the various glycoforms. CHOPa2.4 cells were preferred by the researchers for their comparatively high level of production of tPA. They chose relatively inexpensive, but effective additives for optimizing expression (glutamine, glucose, sodium butyrate, yeast extracts, and bactotryptone). Figures 9, references 22: 3 Russian, 19 Western.

**Recombinant Mouse Cell Lines Transformed by Various Vectors Based on Beef Papilloma Virus Type 1 and Expressing Human Tissue Plasminogen Activator**

937C0142C Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
(manuscript submitted 22 Apr 91) pp 1239-1247

[Article by S. B. Aleshkov, M. B. Ustav, A. A. Bayev, Institute of Molecular Biology imeni V. A. Engelhardt, USSR Academy of Sciences, Moscow; Estonian Biocenter, Estonian Academy of Sciences, Tartu; UDC 57:085.23:577.214.625]

[Abstract] Human tPA, used for thrombolytic activity, can be produced by recombinant lines of cells of mammals, which can ensure the production of a functionally active protein in quantities necessary for clinical use. Human tPA is also a convenient reporter protein thanks to the availability of fast, inexpensive methods for determining its activity, and tPA cDNA can be used for developing new systems for expressing eukaryotic proteins. The researchers here attempted to optimize a system of expression that includes mouse fibroblasts and BPV1-based vectors by modifying individual regions of

the viral genome and flanking sequences. The marker used was a human tPA cDNA transcription unit that enabled the study of several properties of the vectors for tPA expression. The researchers present here the results of experiments involving vector engineering and the use of those vectors to produce recombinant cell lines. They were able to vary certain properties of the vectors by adding a promoter to the regions bounded by a viral DNA sequence and by duplicating the LCR-E6-E7 region. In the event of reverse orientation of the additional pTk promoter in relation to the direction of the BPV1 reading frame, the vectors demonstrate in the transformation of the C127 cells a lowering of focus-forming activity, a considerable reduction in the quantity of episomal forms of vectors, and a worsening of vector properties that is linked to the production of a minimal number of tPA-expressing lines among all the transformants. All that can be explained by transcripts that are antisense in relation to the BPV1 reading frames and that suppress the transforming and replicating properties of the viral genome. Certain properties, however, were improved through the use of the sequence of the L x 1 mutant of BPV1 that includes a tandem duplication of LCR-E6-E7 in combination with the additional pTk promoter for enhancing transcription of the early region of the viral genome. The modified vector demonstrated the greatest number of transformation focuses, and more than 40 percent of the transformed lines expressed tPA. Figures 3, references 25: 2 Russian, 23 Western.

**Reverse Transcriptase of HIV: Cloning, Expression in *E. coli*, Enzyme Purification, and Production of Monoclonal Antibodies**

937C0142D Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
(manuscript submitted 18 Jan 91) pp 1248-1257

[Article by V. O. Rechinskiy, S. F. Barashov, I. L. Degtyarev, S. M. Vorovyev, D. L. Lyakov, A. A. Mishin, D. A. Kostyuk, A. I. Starov, G. R. Matsevich, S. N. Kochetkov, Institute of Molecular Biochemistry imeni Engelhardt, USSR Academy of Sciences, Moscow; Institute of Viral Preparations, USSR Academy of Medical Sciences, Moscow; UDC 577.214.32]

[Abstract] HIV-1 is a retrovirus whose life cycle includes a stage of reverse transcription. The nucleotide sequence that codes reverse transcription is part of the *pol* gene of the virus. As a result of expression, after a series of conversions in the target cell, a polypeptide precursor with a molecular weight of about 100 kilodaltons is formed, and the composition of the precursor includes not only the reverse transcriptase, but also a protease and an integrase (or endonuclease). Autocatalytic processing frees from the precursor the protease, which then specifically splits the precursor, as a result of which all the above enzymes are formed, including a mature form of reverse transcriptase. A number of laboratories have cloned and expressed the reverse transcriptase in various types of cells. In most of the work, the expression vectors contained the part of the *pol* gene that codes the reverse

transcriptase only. The work reported here involved the creation of a reverse-transcriptase producer in which autocatalytic processing was used to produce the enzyme. A genetic structure had to be created that contained in the expressing segment sequences coding both reverse transcriptase and the protease. If the polypeptide precursor that was to be formed was capable of autocatalytic proteolysis, it would be possible to form a mature form of the reverse transcriptase with the so-called proper molecular weights. They were successful in effecting the processing in *E. coli*, but a primarily active form with a molecular weight of 57 kilodaltons was produced, and its properties were different from the viral enzyme. The researchers also managed to produce monoclonal antibodies to the reverse transcriptase. Figures 6, references 22: 3 Russian, 19 Western.

#### Conservative and Variable Regions of Amino Acid Sequences of Snake Phospholipases A2

937C0142E Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
[manuscript submitted 21 Dec 90; resubmitted  
7 Mar 91] pp 1345-1356

[Article by P. V. Kostetskiy, S. F. Arkhipova, R. R. Vladimirova, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow; UDC 577.112.5.087]

[Abstract] The relationship between number of conservative and variable regions and phylogenetic difference of comparable groups of a set of homologous sequences are studied for homologous phospholipase A2 amino acid sequences from 21 snakes belonging to 11 genera of the families *Elapidae*, *Viperidae*, and *Colubridae*. The list of snakes was as follows: *Naja naja naja*, *N. n. atra*, *N. n. kauthia*, *N. n. oxiana*, *Naja melanoleuca*, *Aspidelaps scutatus*, *Hemachatus haemachatus*, *N. mossambica*, *N. nigricollis*, *Pseudechis australis*, *Laticauda semifasciata*, *Notechis scutatus scutatus*, *Enhydryna shistosa*, *Basis caudalis*, *B. gabonica*, *B. nasicornis*, *Vipera ammodita ammodita*, *Trimeresurus flavoviridis*, *T. okinavensis*, *Crotalus adamanteus*, and *C. atrox*. Significant conservative and variable regions were identified graphically via intergroup comparison of the phospholipase A2. Taxons were formed with a phylogenetic tree constructed from paired differences of matched amino acid sequences. The greater the phylogenetic difference, the greater the number of reliable conservative and variable regions. The researchers found that the result of a comparison depended little on the number of representatives of each group, even if one group was represented by only one sequence. The results were used to predict peptide structure for the purpose of producing antibodies specific to the phospholipase A2 of a taxon. Figures 5, references 26: 2 Russian, 24 Western.

#### Study of Topography of RNA Polymerase of T7 Bacteriophage With Monoclonal Antibodies

937C0142F Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
[manuscript submitted 11 Mar 91] pp 1357-1363

[Article by V. A. Pap, Ye. F. Zaychikov, S. M. Vorovye, I. L. Degtyarev, S. N. Kochetkov, Limnological Institute, Siberian Department, USSR Academy of Sciences, Irkutsk; Institute of Molecular Biology imeni V. A. Engelhardt, USSR Academy of Sciences, Moscow; UDC 577.214.32]

[Abstract] The T7 phage RNA polymerase is one of the most studied of transcription enzymes. The enzyme consists of a single subunit that has a molecular weight of 100 kilodaltons and contains 883 amino acid residues with a well-known primary structure. In earlier work, this group of researchers localized the active center of the enzyme via highly selective affine labelling of the T7RP with substrate analogs, thereby demonstrating that the Lys<sub>631</sub> residue is labelled and, consequently, is near the active center. In a continuation of that work, they report here that they produced a panel of monoclonal antibodies that interact with the enzyme. They mapped antigen determinants for four clones of monoclonal antibodies that inhibit enzymatic activity. All the antibodies are shown to bind with the C-region fragment of the enzyme molecule (residue 589-883). In a study of antibody competition, three clones are found to be specific to one epitope, whereas the other clone is specific to a second epitope. The polypeptide chain containing the determinants Met<sup>861</sup>-Ala<sup>883</sup> for the 4H<sub>8</sub> antibody and Met<sup>750</sup>-Met<sup>832</sup> for the 9B<sub>2</sub>, 3H<sub>11</sub>, and 2A<sub>2</sub> antibodies is localized via partial cleavage of the RNA polymerase with cyanogen bromide and subsequent separation of the fragments in PAGE, plus immunoblotting. Figures 3, references 15: 4 Russian, 11 Western.

#### Study of Action of 35S RNA Promoter in Various Organs of Transgenic Potato Plants

937C0142G Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
(manuscript submitted 10 Mar 91) pp 1372-1376

[Article by A. L. Gartel, V. A. Avetisov, G. I. Sobolkova, K. G. Gazaryan, O. S. Melik-Sarkisov, Institute of Molecular Genetics, USSR Academy of Sciences, Moscow; All-Union Scientific Research Institute of Agricultural Biotechnology, Moscow; UDC 577.218]

[Abstract] It has recently been demonstrated that the cauliflower mosaic virus RNA 35S promoter, one of the most popular promoters for the expression of foreign genes in transgenic plants, is not constitutive. The researchers here set out to compare the action of that promoter in various organs of the transgenic potato via fluorometric testing of the activity of  $\beta$ -glucuronidase (GUS) in those organs. Transformation of *Solanum tuberosum* cells was performed on stem parts by means of infecting them with a "disarmed" *Agrobacterium*

*tumefaciens* LBA 4404 strain containing the binary vector pBI121. The plants formed roots and grew normally in a medium with a canamycin concentration of 100-300 µg/ml. In the plants produced in vitro, formation of microtubers was induced, and from them tubers later formed in soil. Fluorometric testing determined that the level of expression of GUS from the 35S promoter was several times higher in the stems than in the leaves of the transgenic potato, suggesting that the promoter is more effective in the stems than in the leaves. The promoter, the researchers concluded, is not inducible. The method advanced by the researchers may be used to study organ specificity and possible inducibility of promoters, but is poorly suited for comparing promoter strength. Figures 1, references 14: 2 Russian, 12 Western.

**Extensin Promotor Is More Effective in Callus Than in Organs of Transgenic Potato**

937C0142H Moscow MOLEKULARNAYA  
BIOLOGIYA in Russian Vol 25 No 5, Sep-Oct 91  
[manuscript submitted 10 Mar 91] pp 1377-1381

[Article by A. L. Gartel, V. A. Avetisov, G. I. Sobolkova,  
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Moscow; All-Union Scientific Research Institute of Agricultural Biotechnology, Moscow; UDC 577.218]

[Abstract] Carrot extensin is the chief component of the cell wall and is rich in glycoprotein oxyproline. The fact that expression of extensin is intensified after a wound or the attack of pathogens indicates that it plays a protective role in the plant. A wound leads to the appearance of transcripts 1.5 kbp and 1.8 kbp in size and coded by the same gene; they have different points of transcription initiation, however. At the same time, treatment with ethylene leads to activation of transcripts 1.8 kbp and 4.0 kbp in size. To study the properties of the extensin promoter, this group of researchers placed the GUS gene under the promoter directing the synthesis of a long extensin transcript in the binary vector pBI and then inserted the plasmid produced into a tetraploid Istrinskiy potato plant by way of an *Agrobacterium rhizogenes* A4 strain transformation system. They managed to produce a transgenic potato root callus from which regenerated transgenic plants were grown. The promoter was found to be more effective in the callus than in mature organs. Figures 3, references 12: 2 Russian, 10 Western.

**Mapping of Vaccinia Virus Genes Encoding p34 and p40 Membrane Proteins by Hybridization-Based mRNA Selection Technique**

937C0125A Moscow MOLEKULARNAYA  
BIOLOGIYA in Russian Vol 25 No 6, Nov-Dec 91  
(manuscript received 12 Feb 91) pp 1492-1496

[Article by N.V. Cheshenko, N.A. Netesova, A.I. Muravlev and E.G. Malygin, All-Union Scientific Research Institute of Molecular Biology, "Vektor" Scientific Industrial Association, Koltsovo, Novosibirsk Oblast; UDC 576.8.098:577.1]

[Abstract] An analysis on genes encoded by HindIII-J and HindIII-F genome fragments of vaccinia virus L1VP involved selective hybridization of the fragments with mRNA isolated from BNK21 cells used for growth of the virus. Subsequent immunochemical analysis of the protein products of a cell-free translation system derived from rabbit reticulocytes demonstrated that the HindIII-J fragment encoded a 30 kD protein identified as p34. The HindIII-F fragment was found to encode a 37kD protein identified as p40. These observations further complement available information on gene sequencing in the vaccinia genome. Figures 4; references 17: 4 Russian, 13 Western.

**Structure of M13 Phage Bearing Chimeric B-Proteins**

937C0125B Moscow MOLEKULARNAYA  
BIOLOGIYA in Russian Vol 25 No 6, Nov-Dec 91  
(manuscript received 19 Feb 91) pp 1497-1503

[Article by G.P. Kishchenko, O.O. Minenkova, A.I. Gruzdev\* and V.A. Petrenko, Scientific Research Construction Engineering Institute for Biologically Active Substances, "Vektor" Scientific Industrial Association, Berdsk, Novosibirsk Oblast; \*Institute of Cytology and Genetics, Siberian Branch, USSR Academy of Sciences, Novosibirsk; UDC 577.322.4]

[Abstract] A series of M13 phages (M13B1, M13BOM1, M13BOM2, M13BOL1) were assessed for effects of chimeric B-proteins (5 exogenous amino acids inserted into the 50 amino acid sequence of the native protein) on M13 structure. The combination of electron microscopy and data on spectrophotometric, circular dichroism and fluorescent spectra demonstrated that the chimeric B-proteins did not affect DNA packaging nor the compact arrangement of viral proteins. Changes in the N-terminus of the B-protein had no bearing on its interaction with DNA, which is essentially a function of the C-end. However, in some cases the central segment of the B-protein rotated with retention of the basic central dihedral angle configuration due to restrictions posed by adjacent proteins in the capsid. Titration with auramine-O revealed that there was no correlation between the number of carboxylic groups on the B-protein and the total number of surface carboxylic groups. Accordingly,

not all B-protein carboxylic groups are exposed on the viral surface. Figures 4; tables 1; references 10: 3 Russian, 7 Western.

**Structure and Function of HindIII-I Fragment of Vaccinia Virus L1VP Genome. Part 1. Cloning of Gene I<sub>5</sub> and Product Identification**

937C0125C Moscow MOLEKULARNAYA  
BIOLOGIYA in Russian Vol 25 No 6, Nov-Dec 91  
(manuscript received 21 Mar 91) pp 1526-1532

[Article by N.A. Netesova, A.I. Muravlev, N.A. Chikayev and E.G. Malygin, All-Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast; UDC 578.821]

[Abstract] Gene I<sub>5</sub> in the HindIII-I fragment of vaccinia virus L1VP genome was cloned in plasmid pUC19, the latter used to transform E. coli JM-103. Immunochemical techniques were then used to identify protein p90 (93.6 kD) as the gene product. The study also revealed that, unlike the case in vaccinia virus WR in which 2 open reading frames are present (H<sub>4</sub> and H<sub>5</sub>), in the L1VP strain p90 is encoded by a single fused reading frame. Although p90 is associated with the core in the L1VP strain of the vaccinia virus, its epitopes are detectable on the surface of L1VP virions. Figures 5; references 12: 3 Russian, 9 Western.

**Structure and Function of HindIII-I Fragment of Vaccinia Virus L1VP Genome. Part 2. Cloning of Gene I<sub>6</sub> and Product Identification**

937C0125D Moscow MOLEKULARNAYA  
BIOLOGIYA in Russian Vol 25 No 6, Nov-Dec 91  
(manuscript received 21 Mar 91) pp 1533-1538

[Article by N.A. Chikayev, A.I. Muravlev, N.A. Netesova and E.G. Malygin, All-Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast; UDC 578.821]

[Abstract] HindIII-I fragment of the genome of vaccinia virus L1VP bearing the I<sub>6</sub> gene was used to construct plasmid pUC19 bearing I<sub>6</sub> for transformation of E. coli JM-103. Immunochemical techniques were then used to identify a specific product of I<sub>6</sub> that behaved on electrophoresis as a 34 kD protein, although the calculated mass was 23.2 kD. This particular protein is lacking in the intact virus, but has been identified in relatively large quantities in extracts of CV1 cell cultures infected with this strain of the vaccinia virus. In general, this particular protein appears to be analogous to the product of the H<sub>6</sub> gene of the WR strain of vaccinia virus. Figures 4; references 16: 5 Russian, 11 Western.

**Comparative Analysis of Nucleotide Sequences of 5'-Terminal and Central Domains of 16S rRNA of Yersinia Pestis and Escherichia Coli**

937C0125E Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 6, Nov-Dec 91  
(manuscript received 14 May 91) pp 1636-1642

[Article by G.G. Dikhanov and O.N. Podladchikova, Scientific Research Antiplague Institute, USSR Ministry of Health, Rostov-on-Don; UDC 579.842.23+577.217.34+57.012.5]

[Abstract] An analysis was conducted on the primary structure of the 5'-end and central domains of 16S rRNA of *Y. pestis*, which bind S15 and S20 proteins, for comparison with analogous data on *E. coli* 16S rRNA. Comparison of the 16-989 bp segments using cDNA cloning demonstrated that differences between the 2 organisms were due to nucleotide substitutions. They have been identified on the surface of the 30S subunit at hairpin turns 6 (11 nucleotide exchanges out of 38 nucleotides) and 18 (10 out of 21), and at binding sites of rRNA for proteins S8, S15, S16 and S20. The since the *Y. pestis* and *E. coli* S proteins differ in electrophoretic mobilities on PAG, there are obviously differences in the

rRNA binding sites of the 2 microorganisms. Figures 5; references 23: 5 Russian, 18 Western.

**Cloning of Genus-Specific DNA Probe of Fusarium Oxysporum**

937C0125F Moscow MOLEKULYARNAYA  
BIOLOGIYA in Russian Vol 25 No 6, Nov-Dec 91  
(manuscript received 4 Jun 91) pp 1667-1669

[Article by B.K. Irisbayev, A.S. Krayev, G.Ye. Pozmogova, A.A. Abdukarimov and K.G. Skryabin, "Bioinzheneriya" Bioengineering Center, USSR Academy of Sciences, Moscow; Institute of Bioorganic Chemistry imeni A.S. Sadykov, Uzbek SSR Academy of Sciences, Tashkent; UDC 577.21]

[Abstract] Genus-specific DNA probes were constructed for *Fusarium oxysporum* via PRC amplification of spacer ITS1 between 18S RNA and 5.8S RNA. The system was rendered efficient and relatively simple by the use of 2 universal primers—TTTCCGTAGGT-GAACCTGCGGAAGG complementary to the 5'-end of all 18S RNA and 5'-GAACCAAGAGATCCGTTGT-TGAAAC representative of the conservative 5'-end of 5.8S RNA in fungi. The resultant 209 bp DNA probe was shown to be specific for *F. oxysporum*. Figures 2; references 8: 3 Russian, 5 Western.



### Some Aspects of the Employment of Liposomes for the 'Deposition' of Neurotropic Preparations

937C0017A Moscow BULETEN  
EKSPERIMENTALNOY BIOLOGII I MEDITSINY  
in Russian Vol 112 No 11, Nov 91 pp 497-499

[Article by A. Yu. Burt, F. M. Lenkovskiy, L. M. Sukhonoshchenko, Yu. B. Abramov, V. I. Sachkov, Scientific Research Laboratory of Problems of Anesthesiology (director—professor V. I. Sachkov of the surgery department), (director—academician of the Academy of Medical Sciences of the USSR M. I. Kuzin of the I. M. Sechenov Moscow Medical Academy; the article was submitted by academician of the Academy of Medical Sciences of the USSR Yu. A. Vladimirov]

[Text] The administration of biologically active substances to an animal organism in liposomal form has a pronounced effect on many pharmacological parameters, such as the dose-effect dependence, the toxic and side effects, the pharmacokinetics and pharmacodynamics, etc.<sup>2-4</sup>

The degree and the site of the bonding of molecules of neurotropic preparations with a liposomal membrane depend on electrostatic and hydrophobic interactions. It is possible to estimate the bonding force of such molecules with liposomes with the use of the nuclear magnetic resonance (NMR) method.

The <sup>1</sup>H NMR line width of amphiphilic substances in the composition of a phospholipid membrane is significantly greater than the line width of molecules which are in the aqueous phase, due to the reduction in the mobility of their molecules. In the case of rapid exchange between the membrane-bonded and the free states of the molecules of these substances they will have a certain intermediate line width, proportional to the membrane-water distribution coefficient.<sup>1</sup>

The employment of this method to determine the force bonding neurotropic drug molecules with the liposomal membrane was considerably facilitated by the fact that the aromatic region of the <sup>1</sup>H NMR spectra of natural phospholipids was transparent, and the molecules of the majority of the preparations employed contain aromatic groups.<sup>1</sup> The fact that there are tertiary amino groups in the composition of the molecules of the majority of the compounds bearing a positive charge at physiological pH values is noteworthy. The addition of negatively charged acidic phospholipids to neutral phospholipids significantly increases the membrane-water distribution coefficient for these compounds.<sup>6, 7</sup> Besides affecting the phospholipid composition of liposomes the structural organization of the preparations (drugs) also affects their rate of output. Thus, small unilayer ultrasound-irradiated liposomes should yield preparations more rapidly than large multilayer liposomes of the same composition. By altering the indicated parameters, it is possible, in our opinion, to vary the degree and the character of the interaction of the preparations with liposomes and, in this way, effectively affect their pharmacokinetics.

The purpose of the present work was to investigate the capabilities of liposomes to prolong the effect of neurotropic preparations when they are administered locally.

#### *The investigational methods.*

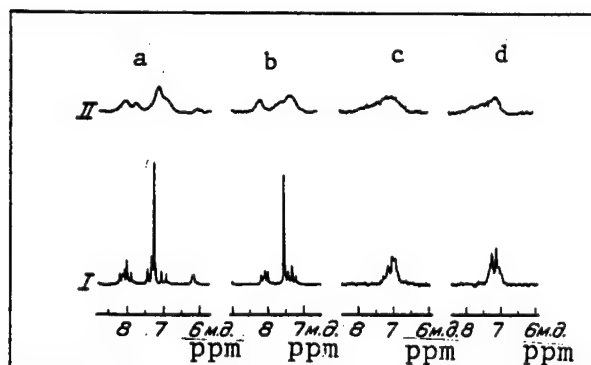
Egg phosphatidyl-choline of the Kharkov Bacterial Preparations Factory and azo-lectin of the "Sigma" company (United States) were used to prepare the liposomes. Medicinal preparations were taken in the form of official solutions (aminazine, tetracaine hydrochloride, novocain, trimecaine hydrochloride of Soviet manufacture; haloperidol, droperidol, pipolphen and lidocaine of Hungarian production; marcaine of the "Bofors, Nobel-Pharma" firm, Sweden). The liposomes for the NMR experiments were prepared in the following manner: a buffer (<sup>2</sup>H<sub>2</sub>O; 0.01 M tris-<sup>2</sup>HCl, p<sup>2</sup>H 6.5; 0.1 M KCl) was added to dry phospholipids (the egg phosphatidyl choline was dried in a rotary evaporator) and was agitated until a homogeneous emulsion was obtained. The obtained emulsion then had argon blown through it for a period of 15 min and then was processed in a UZDN-1 (an ultrasound diagnostic unit) with ultrasound at a frequency of 22 kHz for 15 min. The preparations were dried lyophilically before being added to the liposomes. Official solutions of these preparations were added directly to dry phospholipids to prepare liposomal forms of these preparations for conducting experiments on animals. Unilayer (ultrasound-irradiated) liposomes were prepared in the same way as the liposomes for the NMR experiments. Multilamellar (ultrasound-nonirradiated) liposomes were not subjected to ultrasound processing. <sup>1</sup>H NMR spectrograms were made in the Fourier transformation regime employing an FT-80 spectrometer made by the "Varian" company (United States), at a frequency of 80 MHz.

Investigations of the liposomal forms of the preparations were conducted on white mice weighing 25-30 g and on rabbits weighing 2.5-3.5 kg. Investigations of the duration of catalepsy were conducted on four groups of mice with 16 individuals in each group, and 20 mice in each group were employed to determine the lethality of liposomal forms of tetracaine hydrochloride. Experiments were also conducted to determine the duration of epidural anesthesia on four groups of rabbits with eight individuals in each group.

The duration of the catalepsy in the mice was determined by the method described in work.<sup>5</sup>

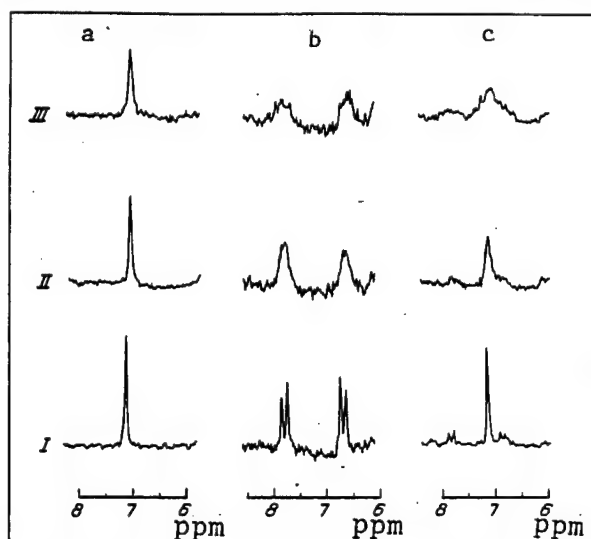
Access to the epidural space of a rabbit was attained, not in the traditional manner through the ligamentous apparatus of the spinal column, but by drilling a hole in the vertebral arch. A catheter with an arresting device was rigidly fixed in the bone to prevent injury (trauma) to the spinal cord. The effectiveness of anesthetization with the employment of epidural anesthesia was evaluated from the variation in the thresholds of pain sensitivity to electrodermal stimulation (EDS) of the rear paw of a rabbit with respect to respiratory, motor, and vocal reactions. The electrodermal stimulations (EDS) were





**Fig. 1. Aromatic regions of the  $^1\text{H}$  NMR spectra of droperidol**

Key: (a) haloperidol (b) aminazine (c) and pipolphen (d) in the buffer ( $^2\text{H}_2\text{O}$ , 0.01 M tris $^2\text{-HCl}$  p $^2\text{H}$  6.5; 0.1 M KCl) in the absence (I) and presence (II) of ultrasound-irradiated liposomes of egg phosphatidyl choline. Note: Mass ratio of preparations to phospholipid 1:10—ppm.



**Fig. 2. Aromatic regions of the  $^1\text{H}$  NMR spectra of lidocaine**

Key: (a) tetracaine hydrochloride (b) and marcaine (c) in the buffer ( $^2\text{H}_2\text{O}$ ; 0.01 M tris $^2\text{-HCl}$  p $^2\text{H}$  6.5; 0.1 M KCl) in the absence (I) and the presence of ultrasound-irradiated liposomes of egg phosphatidyl choline (II), and azo-lectin (III). Note: Mass ratio of preparations to phospholipids 1:10—ppm.

applied via needle electrodes with an MSE-3R electrical stimulator made by the "Nihon Kohden" company (Japan), at a frequency of 100 pulse/s, a pulse duration of 1 ms, in the 1-100 V range. The stimulation time was 1-2 seconds. The respiration dynamics were recorded with an 8-channel "Polyrecorder Model R35 gt" polygraph made by the "officien Galileo" company (Italy).

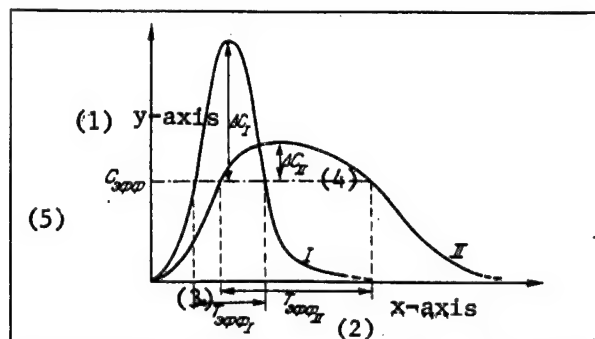
The Rosenbaum nonparametric criterion was used for determining the reliability of the differences in the experiments on the animals.

**Investigational results.** The lines of the protons of the aromatic rings of aminazine, pipolphen, haloperidol, and droperidol in the presence of liposomes of egg phosphatidyl choline were significantly broadened in comparison with the lines of preparations dissolved in water, which attests to the strong bonding of their molecules with the liposomal membrane (Fig. 1).

Its phospholipid composition has considerable effect on the bonding force of the molecules of the preparations with the membrane. Thus, the tetracaine hydrochloride and the marcaine molecules bond with the liposomes of azo-lectin, in whose composition there are about 20 percent negatively charged phospholipids, better than with the liposomes of the egg phosphatidyl choline - neutral phospholipid (Fig. 2). The lidocaine bonds weakly with both membranes due to the insufficient hydrophobic nature of its molecules.

On the whole the results of the NMR investigations show that many neurotropic medicinal preparations possess high affinity for the liposomal membrane, as a result of which the creation of their highly effective liposomal forms becomes possible. Their local application is most promising. In this case the liposomes, remaining a long time at the site of their administration, are not destroyed and are a "depot" for the preparation introduced together with them. It is necessary to note that, besides the pronounced increase in the time of the effect of the introduced preparation, the liposomes can significantly reduce its toxicity, since they should reduce the excess concentration of the preparation (Fig. 3).

In order to estimate the liposomes' prolonging effect we investigated the duration of catalepsy in four groups of white mice. Haloperidol and the droperidol were administered intraperitoneally to the first two groups at a dosage of 25 mg/kg. The duration of the catalepsy in this case was 87q40 min for the haloperidol and 59q33 min for the droperidol. These same preparations at the same dosages were administered intraperitoneally to the 3d and 4th groups in unilayer liposomes of egg phosphatidyl choline (the mass ratio of phospholipid to the preparations was 10:1). In this case the duration of the catalepsy was 288q110 min for the haloperidol and 133q60 min for the droperidol. Thus, liposomes prolong the effect of haloperidol by 3.3 times ( $p < 0.01$ ), and of droperidol by 2.3 times ( $p < 0.01$ ). Moreover, after the introduction of haloperidol in pure form catalepsy ensued in all 16 of the mice after a short but sharply expressed convulsion in all 16 of the mice, but with its administration in liposomal form no convulsion was observed. The latter, apparently, is due to the smoother build-up of the concentration of the preparation in the blood with its administration in liposomal form.

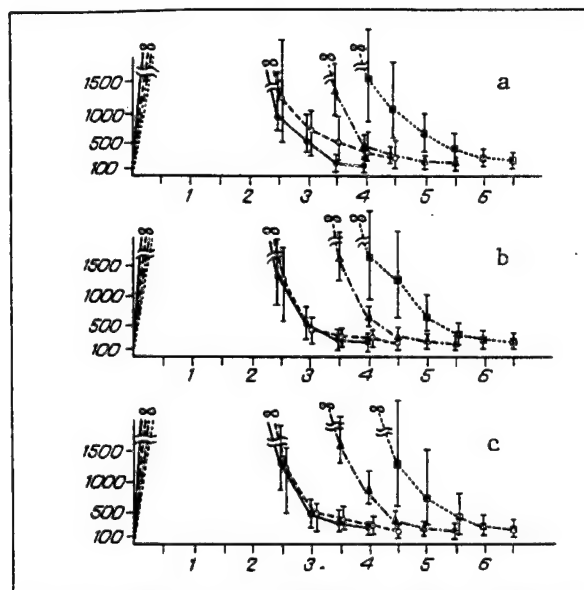


**Fig. 3.** The proposed changes in the concentrations of the preparations at the site of their effect when administered in pure form (I) and in liposomal form (II).

Key: 1. concentration of preparations; 2. time; 3. effect time of the preparations; 4. excess concentration of the preparations; 5. effective concentrations of the preparations

To determine the effectiveness of liposomal forms of local anesthetics we conducted an investigation on rabbits of the duration of epidural anesthesia with tetracaine hydrochloride in liposomes of various composition prepared by various methods, and we compared the toxicity of these forms with the toxicity of pure tetracaine hydrochloride administered intraperitoneally to mice.

When epidural anesthesia with tetracaine hydrochloride (1 ml of 0.5 percent solution) and with its liposomal forms (phospholipids - 5 percent) complete blocking of pain sensitivity developed during the first 30 min after the administration of the preparation and it lasted 120-150 min employing tetracaine hydrochloride in pure form and tetracaine hydrochloride in unilamellar liposomes of egg phosphatidyl choline, 180-210 min with the employment of tetracaine hydrochloride in multilamellar liposomes of egg phosphatidyl choline, and 210-240 min when the tetracaine hydrochloride was administered in unilamellar liposomes of azolectin (Fig. 4).



**Fig. 4.** Dynamics of the variations in pain thresholds with respect to respiratory reactions

Key: (a) motor (b) and vocal (c) reactions to electrodermal stimulation of the rear paw during epidural anesthesia with tetracaine hydrochloride (1 ml of 0.5 percent solution) in pure form (small black circles), in ultrasound-irradiated liposomes of egg phosphatidyl choline (small white circles), in ultrasound-nonirradiated liposomes of egg phosphatidyl choline (black triangles), and in ultrasound-irradiated liposomes of azo-lectin (black squares); Plotted on the x-axis—time (in hours); on the y-axis—pain thresholds (in percent of the background). Mass ratio of phospholipids to tetracaine hydrochloride 10:1.

Moreover, after the expiration of the blocking the restoration of the pain thresholds to values close to the background values, in the case of anesthetization with liposomal forms of tetracaine hydrochloride (especially with liposomes of azo-lectin) proceeded more slowly than anesthetization with the pure preparation. These results agree well with the theoretical assumptions and the data of the NMR investigations discussed above.

#### A comparison of the toxicity of tetracaine hydrochloride and its liposomal forms when administered intraperitoneally to white mice

Numbers in sequence	Experiment (tetracaine hydrochloride in liposomes)			Control (pure tetracaine hydrochloride)	
	composition	tetracaine hydrochloride dosage, mg/kg	lethality, %	tetracaine hydrochloride dosage, mg/kg	lethality, %.
1	Tetracaine hydrochloride 1%, egg phosphatidyl choline 5%	60	40	60	65
2	Tetracaine hydrochloride 1%, azo-lectin 5%	60	0	60	65
3	Tetracaine hydrochloride 1%, azo-lectin 5%	75	45	75	100

The results of the investigation of the toxic properties of tetracaine hydrochloride in unilamellar liposomes of egg phosphatidyl choline and azo-lectin when administered intraperitoneally to their white mice are represented in the table. It is evident from the table that the decrease in toxicity as well as the degree of the prolongation of the effect, correlates with the affinity of the preparations for the liposomal membrane. Thus, our investigation shows the possibility of creating liposomal forms possessing low toxicity and a prolonged effect time. In our estimation the liposomal forms of local anesthetics for long-term regional (nerve-blocking) anesthesia appear to be the most promising.

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**Anticariogenic Action of Bioactive Laminaria Substances on Teeth of White Rats**

937C0113A St. Petersburg FIZIOLOGICHESKIY  
ZHURNAL IMENI I.M. SECHENOVA in Russian  
Vol 77 No 12, Dec 91 (manuscript received 15 Jul 91)  
pp 50-55

[Article by Yu.A. Fedorov and V.A. Drozhzhina, Chair of Therapeutic Stomatology, Institute for Advanced Training of Physicians imeni S.M. Kirov, Leningrad; UDC 612.311.1+616.314.002-053]

[Abstract] Wistar rats maintained on a cariogenic diet from the age of 30 days for 1.5 months were used in studies on anticariogenic efficacy of laminaria extracts. Daily treatment of the teeth with special toothpastes showed that best results were obtained with a formulation including 5 percent laminaria extract and 1.2 percent calcium glycerophosphate. Almost as effective in caries prevention were pastes containing 3 percent mineral-vitamin laminaria concentrate, 5 percent laminaria extract, or 3 percent saponified laminaria concentrate + 3 percent mineral-vitamin concentrate. On tentative grounds, efficacy of the laminaria components was attributed to enhanced remineralization. Possible beneficial effects of vitamins and mechanical stimulation of teeth during treatment were not excluded. Tables 5; references 19: 16 Russian, 3 Western.

**Opioid Mediation of Antinociceptive Effects of Hypothalamic Reward Centers**

937C0113B St. Petersburg FIZIOLOGICHESKIY  
ZHURNAL IMENI I.M. SECHENOVA in Russian  
Vol 77 No 12, Dec 91 (manuscript received 27 May 91)  
pp 15-19

[Article by I.P. Butkevich, V.A. Mikhaylenko and V.G. Kassil, Laboratory of Ontogenesis of Higher Nervous Activity, Institute of Physiology imeni I.P. Pavlov, USSR Acad. Sci., Leningrad; UDC 612.826+577.151.17]

[Abstract] Mildly sedated 41-60 day old rabbits were used in an electrophysiological analysis of opioid mechanisms in antinociceptive action of hypothalamic reward centers. Analysis was based on modulation by intravenous naloxone (0.1-1.0 or 5.0-10.0 mg/kg) of the inhibitory effect of electrical stimulation of reward centers on pain-evoked potentials (EP) in the thalamic parafascicular complex. In control studies naloxone had no effect

on EPs, but low doses of naloxone attenuated full antinociceptive action in four of six rabbits and high doses in one of four. In cases of weaker stimulation of reward centers and incomplete EP inhibition low doses of naloxone potentiated antinociception and led to complete EP inhibition in three of six rabbits. However, high doses were without effect in five of seven rabbits. The mechanism(s) of action of naloxone are hard to interpret, but obviously involve interplay with presynaptic opioid receptors which facilitate antinociception and postsynaptic receptors that attenuate antinociception. In addition, stimulation of the reward centers also alters neurotransmitter balance, indicating that both direct and indirect opioid mechanisms are involved in the hypothalamic antinociceptive system. Figures 2; references 13: 2 Russian, 11 Western.

**Nonspecific Modulation of Higher Nervous Activity in Animals by Neurotransplantation**

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ZHURNAL IMENI I.M. SECHENOVA in Russian  
Vol 78 No 2 Feb 92 (manuscript received 04 Jan 91)  
pp 8-12

[Article by V.L. Silakov, L.A. Moiseyeva, P. Podachin, Ye.A. Lushchekina, Yu.S. Dmitriyev, F.N. Makarov and Yu.V. Balabanov, Laboratory of Primate Behavior, Institute of Physiology imeni I.P. Pavlov, USSR Acad. Sci., Leningrad; Institute of Higher Nervous Activity and Neurophysiology, USSR Acad. Sci., Moscow; UDC 612.821+578.089.843]

[Abstract] Human cortical tissues and their cultures obtained from 8-10 week old cases of induced abortion were used for transplantation into frontal lobes of two mature rhesus monkeys and 18 BD-IX rats. Histologic examination of the monkey brains three months later showed sequestration of the implants by glial scar tissue and destruction. However, the transplants remained viable in two rats. Despite lack of graft viability in most of the rats, observation on behavior and conditioned avoidance testing one month after grafting were indicative of a persistent change in higher nervous activity. Recipient rats behaved in a more emotional manner and exhibited a higher degree of generalized motor and orienting behavior. In general, transplantation was felt to be an adequate model for assessing nonspecific neurochemical effects of human neural tissue on higher nervous activity of other species. Figures 3; tables 1; references 2: 1 Russian, 1 Western.

**Neuroendocrine Function and Behavior of Dogs After Administration of Corticotropin Releasing Hormone (CRH) Into Caudate Nucleus**

937C0113D St. Petersburg FIZIOLOGICHESKIY ZHURNAL IMENI I.M. SECHENOVA in Russian Vol 78 No 1 Jan 92 (manuscript received 25 Jun 91) pp 29-34

[Article by V.V. Rakitskaya, N.L. Voylokov, I.A. Garina, N.F. Suvorov and V.G. Shalyapina, Laboratories of Physiology and Pathology of the Endocrine System and of Higher Nervous Activity, Institute of Physiology imeni I.P. Pavlov, USSR Acad. Sci., St. Petersburg; UDC 612.018+612.822+612.826]

[Abstract] Trials on six male dogs, 20-22 kg, demonstrated that direct microinjection of 10  $\mu$ g of CRH into the caudate nucleus evokes profound endocrine and behavioral changes. Within 30 min of injection blood cortisol levels increased 5-fold, rising to a 10-fold elevation in 60 min vs. control levels. Blood vasopressin peaked in 30 min, falling by 60 min to approximately twice the baseline level, while epinephrine rose to twice the baseline level in 30 min and then plateaued. Norepinephrine, rose 5-fold in 30 min, declined thereafter but remained several-fold higher than baseline concentration. Concomitantly, the dogs exhibited marked increase in targeted and random motor activity and evidence of profound emotional stress. Physiological manifestations of the latter included hyperventilation, rapid pulse rate, and elevated blood pressure, the latter persisting for two hours. In general, these findings indicate that the caudate nucleus is one of the sites of action of CRH since the dose was low enough to be entirely localized. The general

effects encompassed activation of adrenocortical, autonomic and behavior-controlling systems. Figures 3; references 19: 6 Russian, 13 Western.

**Low-Level Microwave Interaction With Cardiovascular System of White Rats**

937C0113E St. Petersburg FIZIOLOGICHESKIY ZHURNAL IMENI I.M. SECHENOVA in Russian Vol 78 No 1 Jan 92 (manuscript received 17 Apr 91) pp 35-41

[Article by I.L. Pomekhina, G.N. Akoyev, L.D. Yenin and V.D. Oleyner, Laboratory of Reception Physiology, Institute of Physiology imeni I.P. Pavlov, USSR Acad. Sci.; Department of Radiotechnical Measurements, Center of Standardization and Metrology, St. Petersburg; UDC 612.1+538.56]

[Abstract] Male Wistar rats, 180-200 g, under hexenal anesthesia (0.25 g/kg) were employed in an assessment of low-level microwave effects on the cardiovascular system in terms of the R-R interval on EKG. Dorsal exposure of the animals at the level of the first five thoracic vertebrae for 20 min or 3 h to low-intensity microwave irradiation (53-78 GHz; 0.75-7.81 mW/cm<sup>2</sup>) did not affect body or skin temperature. However, significant variations were recorded in the R-R intervals regardless of exposure time, especially at 55 and 73 GHz. In addition, 25 percent of the animals died suddenly after 2.5 hours of exposure to 55, 61 and 73 GHz frequencies. Accordingly, cardiac arrhythmia evident in the coefficient of variation of the R-R interval was attributed to a direct action of the low-level microwaves on cardiac conductivity. Individual animals lacking the physiological capacity for adaptation to the effects of the microwave environment on the heart succumbed. Figures 4; references 20: 17 Russian, 3 Western.

**Siemens Enters Tatarstan Pharmaceutical Market***937C0106A Kazan SOVETSKAYA TATARIYA  
in Russian 08 Sep 92 p 1*

["Siemens Conquers Market in Tatarstan". First paragraph is SOVETSKAYA TATARIYA introduction in boldface.]

[Text] This past week negotiations were held in Kazan by representatives of the well-known German company Siemens and directors of the Kazan medical establishments and industrial enterprises.

Siemens has already supplied medical equipment for hospitals and clinics in Tatarstan. During this trip R. Andersen, deputy director of the Moscow bureau of the company, and R. Lind, section director of this bureau, discussed matters of supplying X-ray and ultrasound equipment, a computer tomograph, and equipment for exploring vessels for the newly constructed clinic, which doctors are calling "Tuishevskoy" (in name of its chief physician).

Siemens was founded in 1891. Interestingly, its first foreign office was opened in 1902 in St. Petersburg, and today the ties of German businessmen with the republics of the former Union continue. A joint venture has been founded in Kiev to manufacture computer tomographs.

Siemens develops and produces not only medical technology and instruments, but also electrical equipment. The company has four departments and an annual capital turnover of 50 million dollars. There are more than 400,000 people working in medical technology alone. Siemens headquarters is located in Munich, and it has representatives in many countries of the world.

The fact that Siemens is planning to open its own permanent office in Kazan indicates the serious intentions the German company has of conquering our market. It is true that for now the cooperation will be on the level of buying and selling medical technology. The representatives of the company are still talking very cautiously about more serious cooperation, such as the creation of joint ventures. Nevertheless, R. Andersen promised that the leadership of the company would very attentively review the plan for the organization of a joint venture at the Kazan Medical Instrument Plant. After visiting this enterprise the guests were convinced that there are the equipment, skilled personnel, and free production area necessary for manufacturing medical technology.

In speaking of the perspectives for cooperation, R. Andersen emphasized that the lack of legal guarantees protecting foreign investment, the non-market policy of the Russian Foreign Economy Bank, the bureaucratism of the authorities, and a number of other obstacles are restraining foreign businessmen. It is true, he added, that the beginning privatization is instilling hope. And, in spite of all the minuses of our economy, Siemens is

striving to be the first to enter the domestic market of our republic. Anyway, he who does not risk, does not gain.

**Ukrainian Health Minister on Insurance Law***937C0107A Kiev PRAVDA UKRAINY in Russian  
28 Nov 91 p 4*

[Article by Yu. Spizhenko, Ukrainian Public Health Minister: "Free Medicine is Worthless Medicine".]

[Text] The "Law on Public Health Protection", will soon be discussed in a second reading in the Supreme Soviet. But the discussion is actually about a new law in both content and name. For now it is "Fundamentals of Health Protection Legislation". While generally supporting such an approach and approving individual sections of these fundamentals, as the minister I should state that the fate of this plan will be the same as that of the previous one. Even if it is passed by the Supreme Soviet, our hopes will not be justified. Why?

The sphere of this law, or the "Fundamentals of Legislation...", is one of the most important and most delicate social spheres of society. This is why it needs a strong constitutional basis. This means that if it has not been defined by the Constitution, we will not even be able to pass the proposed fundamentals of legislation in public health service. In the plan of the new constitution, we did not get the constitutional basis necessary and adequate for present and future realities for legislation in the public health service sphere.

The market orientation of our economy is rooted in the previous legislative acts and draft of the Constitution. At the same time, large groups of society, including medical groups, are insistently demanding change in the principles of financing public health service itself and supporting the introduction of medical insurance.

It seemed that we would be able to do everything as before, as it was for 70 years. We, physicians, need not be embarrassed, but could be proud of the old public health system as it was, with the funds allocated by the government.

But we will not forget: A person does not care how or where we get our funds. He wants, without any doubt, to have the right as a taxpayer to quality for medical care. The doctor and medical worker also want and have the right to a valued place in society, including a worthy salary; however, this is not even the main thing for the physician, by virtue of the humane specifics of his profession. The most important thing for him is to be able to perform his professional duties fully.

The physician is experiencing a psychological drama in the present grave situation, and it cannot be otherwise when he loses a patient, one that two or three years ago he calmly not only treated, but cured. That is, our patients did not simply die, but were healed with the help of a doctor.



Now, try to put yourself in this doctor's place, when there is a shortage of drugs, which were recently in good supply, and which are now rendering him powerless against disease and death.

Market principles begin operating, prices are lifted, and even drugs have not avoided the total shortage. The market, in no way free, but rather "black", has all kinds of medicines. But after all, medical care and public health establishments can in no way blend into market relations. This has already been done in principle.

Throughout all the world and many centuries of the development of humankind, medical care was and remains paid. It is so in the maximally commercialized America, as well as in socially oriented Sweden. Medical insurance in all countries is the only way to pay for medical services, although it is accomplished in different ways: by means of a primarily government budget (as in Canada, England, and Sweden) or directly from private funds (as in the United States). But, I repeat, medical services were and remain a good in a market system, with all the aspects inherent to a good, and with all that stems from it.

Therefore, when raising the question of medical insurance and reforming the financing of medical measures for health protection, we need to begin by defining this starting point. It is written in the draft of the Constitution that medical care in the Ukraine is free. But if that is so, then the proposed "Fundamentals of Legislation..." which contains points on medical insurance and the multiple mode of production of the economics of public health service, totally loses its meaning.

Yes, the line about free medical care looks extremely enticing in a social aspect. But it only looks that way. In reality the principles of accessibility, equality, and social justice in obtaining medical care come down to nothing.

Neither the aspects of the goods nor the payment of medical care can have any relationship to social policy. They can be based only on the principles of finance, only the economics of public health service itself.

For the citizens we should and can maintain the usual situation: offer the necessary medical care to each. The patient does not care who (the government or an insurance company) or how much they will pay for this care. It is with this objective that a health insurance system has been introduced into all countries. It is by actually putting this system into practice that the principles of accessibility, equality, and social justice in obtaining medical care will be realized.

That is, there is no conflict between paid medical service and free treatment. After all, even now we, the citizens, are completely paying for the public health system with taxes. But in this case the "address" of the payment is lost, as well as the relationship to its specific medical service. Along with this is the effectiveness of financing. It is even more so under market conditions. Such financing, on the other hand, depends completely on the

capabilities of the government budget, and they are limited, especially now. I will note: the World Bank and International Fund recommend decreasing budget allocations for public health in the next year by 20 percent. Yes, we understand that this is a forced step, in the name of developing our government. Nevertheless, we and our patients cannot remain hostages of budget problems.

Based on all of this, it is suggested that we somewhat alter the order of priority of our legislation.

We need to first formulate a respective section of the Constitution and submit for the consideration of the commission and Supreme Soviet the "Law on Health Insurance and Financing Medical Care in the Ukraine". Then in accordance with them and the new Constitution adopt the "Fundamentals of Legislation in Health Protection".

In this connection, the question will be reasonable: where was the ministry until now, and why are these proposals being made only today, rather than a year ago? I am convinced that it was an objective need to experience during the past year the pathway of searching, doubts, errors, and based on the experience of others—Russia, Estonia, Hungary, Czechoslovakia, and Slovakia—become convinced of how difficult and delicate the problems are that we are solving and of how carefully we should avoid serious errors and unfounded steps.

There will be many fewer mistakes if we place the interests of the citizens as the foundation of our actions in legislation and reform of the public health system, rather than the problems of the department and the interests of the public health systems and its colleagues. That is, the civilized logic accepted throughout the world, on which human rights rest.

This is why we are suggesting to begin at the logical starting point: with the proclamation "Declaration of Health of Ukrainian Citizens", a document which defines the basis of our medical ideology and policy.

The Ministry of Public Health as an administrative structure should not propose its own alternatives for the Constitution or individual laws. These documents can only be the result of the work of society, policies, and parliament. Therefore, we, the physicians, are also proposing the "Declaration..." But at the same time, based on the "Declaration", the Constitution, and the laws we are developing a doctrine of public health in the Ukraine and the concept of the public health system, and in accordance with them a National Public Health program. This is the ministry's business.

The chief intention of the Ministry of Public Health is to be a Ministry of Health, not a ministry of treating illnesses (which is currently 97 percent of the problems that we solve). The Ministry of Public Health is not a republic bureaucratic machine that only allocates finances, resources, and staff and issues directives, but a government guarantor of the right of citizens to health.

**Future plans of the Ministry include:**

- changing scientific priorities, and the first step in this direction will be the creation of a National Institute of Health;
- training new specialists in the field of public health, health insurance, and medical management, as well as family doctors, who would be oriented not only and not so much at diseases, as at the formation of health in their wards;
- forming a health insurance system that is new to us. With this objective a territorial experiment is taking place, and we are searching for and hiring qualified foreign partners who are oriented at solving our problems.

One of the most complex tasks under the new conditions is defining the role of on-site management structures in the public health system and the fate of the therapeutic and prophylactic establishments and medical personnel.

The problems are very important and complex, but they can be solved. Success depends on what legal basis we act upon.

**Working Group Studies Insurance Alternatives**

937C0107B Moscow DELOVOY MIR in Russian  
27 Aug 92 p 6

[Article by Aleksandr Pilenov, "Medical Insurance: Possible Alternatives". First paragraph is DELOVOY MIR introduction in boldface.]

[Text] The desire of many insurance companies to solve objectively the problems of human health protection are fully explicable: Medical insurance is the most widespread in the world.

However, in most cases the good intentions did not go any further. In Dnepropetrovsk, for example, the insurance companies "Ajax", "Dina", and a number of others tried to create such systems. But for some reason there were no results. The "Ukraine" association also made a number of attempts: under the pretext of insurance it tried to add some sums to the beggarly salary of the physicians.

Today the situation has changed somewhat. The medical insurance company "Modstrakh-Dnepr" is proposing a number of interesting developments. They promise to offer the workplaces (the insurer) the right to choose insurance collectively, with the specific allocation of funds of the insurance by employee, the granting of favorable conditions of insurance, etc. Trade unions are trying to join medical insurance. There are odd ideas, and more rarely individually well-thought elements of their implementation. However, we do not yet have a whole concept of medical insurance, which would encompass universal approaches to the problem of human health protection. A working group of the "Ukraine" association is occupied with the formation of

such a concept that would be simultaneously acceptable to both patients and physicians.

"Our goal is to find the best solutions for insuring the responsibility of the physician and protecting the material interests of both the physician and the patient," says Vladimir Brodskiy, general representative of the union of insurance organizations of the "Ukraine" association. "When going to the doctor, a person should know that the doctor bears the responsibility for his health. But at the same time the doctor also needs protection. In my opinion, these concepts should underlie the whole program. After all, these are the principles of world practice."

It also gives preference to the working group of the association. We know that in the world there are two medical insurance systems that are most often used: medical services are either paid for by deductions from a person's salary, or special medical funds are created where a person deposits money for treatment. However, Vladimir Brodskiy is convinced that neither of the systems can work under our conditions. In the first place it is most likely that the government manages mandatory medical insurance and thereby deprives us of choice. In the second place, very few people can save for a rainy day. And there is little hope for the medical establishments at the workplace that even now bear no responsibility for the morbidity level or traumatism at their factory or shop. In general, medical cooperatives, which have no statistics on treatment effectiveness, offer no guarantees of strengthening human health. The advantage to all of this here is that considerable sums of money bypass the funds, which causes the local budget to suffer."

What does the "Ukraine" association offer?

The solution is very simple: introduce medical insurance. The calculations between the medical establishments of alternative medicine and the patients should be through a check through a medical insurance system where the patient of the medical establishment is at the same time also a client of the insurance company. That is, a peculiar checkbook is issued to a person and a single medical card is issued at the same time, which at that point is canceled and automatically becomes an insurance policy. It insures the person against unqualified treatment or side effects associated with such treatment. If, for example, a patient pays a given sum for medical services, but does not receive any benefit from the treatment, then the patient is compensated from the doctor's pocket, say ten times more than he paid for the services.

Incidentally, this system should not be regarded as actions aimed against the doctor. To the contrary, the insurance company may allocate some funds (up to 60 percent) to the doctors that are skilled and conscientiously perform their duties for improving the equipment base. Moreover, the doctors themselves determine the level of their qualifications and here the principle

directly snaps into action: The higher the doctor's skills, the higher his possible material compensation. But at the same time doctors with such a skill level will also pay more out of their own pocket if it is their fault that a victim suffers. Understandably, many physicians in this case will try to set their plan too low. These are the ones who are not sure of their actions. The skilled, qualified physician will be interested in making his plan meet his level, since it is by this plan that he will be able to, for the first time in his life, receive what he has actually earned.

The budget also favors this: Paying in cash will be eliminated in medical establishments, and the funds will go only towards transfer. That is, this is an alternative where the doctor is interested in the quality of his work, the patient is interested in the actual protection of his health, and the budget is interested in guaranteed replenishment of funds. Supporters of the novel idea are convinced that it will provide a real opportunity for the entire medical field to very quickly move into commercial ranks. It is one that people will be able to afford and will operate based directly on this. It is true that solving the problems of medical insurance in the Ukraine is not that simple. And this is why. Two documents—a bill for regulating insurance activity and a bill on medical insurance, both of which should be in line with one another, in reality have little in common and at times are completely contradictory. The bill on medical insurance doesn't even stipulate a financing system. All of this evokes some worry on the part of the Ukrainian League of Insurers, including the State Insurance. We need to eliminate these defects and gaps while there is time.

"Specialists of the 'Ukraine' association are convinced that the concept of medical insurance can only be created jointly," says Vladimir Brodskiy. "That means we need to combine the efforts of all interested parties. We extend an invitation to all who desire to become involved. At the same time, also, there is a need for the establishment of a collective information center, in which the working group wants to collect all the information on the theory and practice of medical insurance in the world. For this we are requesting that all who have such literature or know where to buy it to inform us. We will get it. Due to the wealth of the collective information center, all interested insurance companies will be able to use it."

**Interview with Official of New Insurance Association**  
937C0107C Moscow NEZAVISIMAYA GAZETA  
in Russian 11 Sep 92 p 6

[Interview with Viktor Gorodetskiy, vice-president of the Russian Association of Medical Insurance Organizations, by Vladimir Gurvich; place and date not given: "We Will Insure Health Inevitably". First paragraph is NEZAVISIMAYA GAZETA introduction in boldface.]

[Text] The law "Medical Insurance for the Citizens of the Russian Federation" will enter into force 1 January 1993. The insurance companies should be the most

important element of this system. The Russian Association of Medical Insurance Organizations was recently founded. Its vice-president, candidate of medical sciences Viktor Gorodetskiy, believes that at this level of the development of national public health, medical insurance is the only medicine for the collapse.

[Gurvich] One still wants to ask whether the need for creating the association has really come to a head. There are too many such organizations arising at present, and so far we do not see any results.

[Gorodetskiy] First, I would like to say that there are more than 50 medical insurance organizations in the association, of the approximately 200 that are registered in Russia. There are 20 more that have petitioned for membership. In addition, the number of them is increasing almost daily. This suggests that the time has come for such an organization. The other question is, what are our objectives? There is less than six months remaining before the law on medical insurance is enacted. If we let this process drift without doing the necessary preparative work, the document will become a meaningless declaration. The situation in public health became critical long ago; suffice to say that it was financed at 30-40 percent. The situation has reached strikes among medical personnel. I myself am a physician, and understanding the situation, at the same time I never supported their demands for an increase in salary. A physician should not ask the government for money. The government does not even have it. Rather, he should demand the rapid creation of a health protection system for the citizens that would steadily improve his financial situation.

[Gurvich] Let's assume that a sufficient number of insurance companies are created and the mechanism of medical insurance itself is initiated. Can we adequately predict how it will work and all possible consequences?

[Gorodetskiy] There is one paradox in our medicine. In the West there is one doctor for every 10,000 persons. In the former USSR there are 46-50, and in Moscow there are 93-96. With such a high number of medical hands, the level of national public health service is much lower than that of the West. Here, all who have the respective diplomas are considered doctors. But after all, it is no secret that many of them de facto are not. I can give you an example from my own practice. When I was chief physician, I had a female colleague that I sent home on heavy days and saw the patients myself. The insurance companies are intent on intervening in this situation. As guarantors of the quality and level of medical care to the citizens, they are objectively interested in improving the service of their clients, which presupposes that physicians will perform their work at the highest professional level.

[Gurvich] There is resistance to the introduction of medical insurance. In your opinion, what are the sources of this resistance?

[Gorodetskiy] There is a very inert, conservative structure to our medicine. In order to make the system really work, we need to give therapeutic establishments the status of an independent legal entity, for example in the form of a municipal enterprise. These enterprises will be allocated a portion of the necessary funds from the budget, but the rest they will have to earn themselves. This will permit them to become equal partners with full rights in the medical services market. As a result, the role of chief physicians will radically change, from that of administrators and mediators between rayon public health services and their own collectives, to becoming medical managers. But most of them are completely unprepared for this. Hence, sabotage on their part. The most hostile to the innovation of the bureaucratic personnel is he who understands that he will be superfluous in the new system. His primary duty—budget allocation—will disappear. I generally believe that the transition to medical insurance necessitates demarcation of authority in the public health field between the four participants in this process—the patients, the therapeutic establishment, the medical insurance organization, and the state management agencies. A strictly limited number of functions should be maintained for the latter. It is the strategic planning of the development of the branch, training of specialists, and the development and implementation of nationwide programs (such as controlling AIDS), and epidemic prophylaxis. The remaining problems can be successfully resolved by other participants of this process. This will accelerate the formation of a market of medical services. Unfortunately, instead of placing all the insurance organizations at equal starting positions in the developing market and forcing them to compete, it is suggested that a government insurance fund and government insurance companies be created, which would have a privileged position from the beginning. This not only violates the anti-monopoly legislation and the law on medical insurance, but it also basically kills only the growing market relations in medicine.

[Gurvich] But shouldn't the government itself think about these matters and establish favorable conditions for the activity of the insurance companies?

[Gorodetskiy] For now the situation is contradictory. For example, in Russian Presidential Resolution No. 41 on the implementation of the law on medical insurance, there is a list of documents that are necessary for the insurance companies to get licensed. There are seven for mandatory insurance, and five for voluntary. However, the Ministry of Finance requires an additional packet of documents, and instead of the stated one month, it takes six months for many companies to get registered.

### Health Insurance in Kazakhstan

937C0107D Alma-Ata KAZAKHSTANSKAYA PRAVDA  
in Russian 29 Aug 92 p 5

[Article by M. Tulepbayev, candidate of medical sciences: "What Kind of Insurance Should We Adopt?" A critical look at the health insurance model adopted in Kazakhstan. First paragraph is KAZAKHSTANSKAYA PRAVDA introduction in boldface.]

[Text] Medicine has followed the path to radical economic reforms in the beggarly clothing of residual financing. Expenditures on public health last year were (at current market prices) 3.5 billion rubles, which is an average of 208 rubles per person. There is one solution: it is necessary to find a different mode of operation for the branch, which would indispensably include the market elements. I believe the best solution for our activity would be a combined, budget-market model, in which the insurance principle of the formation of financial resources is an additional, to compensate the shortage of budget allocations.

The principle "raze it to the ground, and then..." does not apply here. During the transition we cannot even to the slightest degree take the risk of further reducing the level of public health and the accessibility and quality of medical care. After all, the status of public health in the republic has already reached a dangerous point, beyond which degeneracy occurs. An actual genocide has been going on against the Kazakh people for decades. Nuclear test sites, the Aral... The people breathe toxic air, eat food which in its variety, composition, and quality can in no way be called balanced, drink water saturated with chemicals and dirt, and live in apartments that were not designed for comfort. Most of them work in conditions that do not meet sanitary norms. Now of one thousand newborn children, more die than of a thousand lambs.

The health of the people is the nation's wealth. This is well understood in the United States, for example. And it is quite right that it has become a tradition for the President to address the health of the nation in an annual public speech.

Many postulates from the sphere of material production are also now found in public health. Thus, the "new economic mechanism" is confronted in the health insurance field. I see the ersatz nature of this mechanism in the fact that the residual principle of financing the branch remains under conditions of increasing inflation. It is similar to a check system, with success that failed in agriculture. For a mere morsel the relationships of the medical personnel at the polyclinic and hospital become aggravated to the point of conflict, often to the detriment of the health of the patients, with all the attendant consequences. But after all, the economic form of public health activity should be directed at the production of financial resources rather than redistribution.

I support medical insurance as one of the forms for the organization and payment of medical care. But I am also convinced that it should not be introduced in one fell swoop. It needs to be considered with the following real, objective factors:

- an insurance agent institute has not been formed. Today's insurance company has placed profits as the basis of its operation, rather than improving public health;



- the level of supplies and equipment support and qualifications of medical staff in the therapeutic establishments will provide medical care to the insured;
- the economic categories for the medical establishments are strange, little known, and practical developments in these matters are very meager;
- 70-90 percent of the branches of material production are unprofitable;
- in a society in which the proportion of non-working persons (children, students, retirees, the disabled, unemployed) or those working in budget and unprofitable organizations is large, the entire weight of insurance contributions lies in the budget of local government agencies;
- ideas of medical insurance are not supported by the leaders of the branch, since they are afraid of losing their power. They are ready to accept medical insurance, without changing anything. However, you can't go forward without moving.

The introduction in 1993 of mandatory medical insurance for the entire public will result in a sharp deterioration in medical care to the public. We need to thoroughly review not only the concept, but also the methods of putting it into practice.

A model of medical insurance is based on several "whales". It is a basic program according to which each of us will receive some selection of free medical services. The government budget will finance it for the unemployed; the workplace will finance it for their employees. The proposed model will not have the anticipated effect. First, the ratio of paid and free forms of medical care is vaguely reflected, it is not clear who and how the volume of necessary and additional medical services will be determined. Moreover, the employees of budget organizations and retirees are in a sad position today because they are dependent on the "fat purse" of the government.

The deduction by the workplace of eight percent of their resources for the needs of public health is a lot, if we measure by yesterday's standards. But it is little by today's standards, and even less by tomorrow's. This sum will be "driven" into the cost of goods and services. And if we take into account that the increase in the cost of the goods by three percent will make its ability to compete questionable, the factory's already unenviable position that it is presently in will become worse.

Moreover, the dual burden of expenses is lying on the workplace. They have to pay the contributions for mandatory insurance and also pay from the social funds for the treatment of their employees, since they will not be able to afford it. Even today it is clear that the cost of complex operations will be tens of thousands of rubles.

In order to not beat the splendid idea of medical insurance to the ground, I propose two alternatives.

The first alternative is to extend the transition to mandatory medical insurance prior to economic recovery of this branch of the national economy. Initiate and

develop only voluntary medical insurance for citizens and the workplace. Only in this case the workplace is not threatened by dual expenses, but each insured will be personally interested in protecting his own health.

During this transition period the public health service will be financed primarily by the government based on a calculation per person per year, which is a guarantee of medical care to all of the public without exception. The principal aspect should be that these allocated monies are not given to the therapeutic and prophylactic establishments, but rather to the medical insurance organizations which finance the medical establishments in accordance with the effectiveness of their work and demand for it.

The second alternative is to begin mandatory medical insurance only for the non-working—the retirees, disabled, children, and students, entrusting their care to the government to allocate resources from the budget and pension funds and civilian social security. The entire working public should conclude agreements for voluntary insurance. This is where the lion's share of expenses are and the employer can bear the responsibility for them himself.

With mandatory medical insurance, the territorial management agencies will determine the volume of medical care. But we can foresee even now that this volume will not be very large and that medical personnel will be occupied with self-orientation, at times to the detriment of the patient. Will the client be able to obtain effective treatment and service when ill? I am not sure. Therefore, it makes more sense for the workplace and citizens to sign agreements for voluntary medical insurance with broader possibilities of obtaining skilled medical care. It is important to note that these medical insurance organizations are very interested in the quality of treatment and the prevention of diseases, since they bear the legal and financial responsibility of their clients for the results of therapeutic measures.

However, the lack of a regulatory law and supervision makes it possible for anyone who desires to do so to become involved in the medical insurance field. Therefore, the law needs to determine the order for creating medical insurance organizations and set the minimum authorized capital and requirements for the level of payment ability. The law should stipulate that all medical insurance establishments are obligated to publish account balances and a profit and loss account for the past calendar year. In order to create a "civilized insurance market" we need to introduce a system of guaranteed assets for compensating the financial losses of the insured in cases of bankruptcy of the medical insurance establishments. In order to operatively solve these problems, we need to create a central agency for medical insurance supervision with the respective structural branches in the oblasts and rayons.

Naturally, the government budget will not be able to establish the optimal level of financial support for the public health service at present. It is presently one-third of the optimal. The other two-thirds can be sought by

various means. This is most correctly done in accordance with the laws of market economics using the following two mechanisms.

The essence of the first is to institute simultaneous or gradual privatization of some of the state public health service property. Subject to privatization should only be the material resources that have paid for themselves or which have substantial wear; they have greater "financial weight" in the process of use. The privatized portion of the property should be 50 percent. In this manner the budget is immediately doubled without additional subsidies, due to income from sales and lease.

Secondly, another one-third is still needed in order to reach an optimal budget. This is the financial part and should mandatorily play the role of an active economic activity stimulant for the public health service. For this we need to create a market mechanism for the implementation of the results of medical labor. In general, it may look like a transition of government medical establishments to inter-branch cost accounting. The medical service will be organized according to agreement with the workplace and establishments with subsequent payment for services rendered in accordance with the presented account. Prices are set based only on 30 percent of the budget, that is, financial proceeds according to the agreements should cover the remaining third of the optimal budget. This mechanism may also be built on the basis of voluntary insurance of the employees, that is, medical insurance premiums will be low (within the framework of the third part of the budget), and that means profitable and advantageous.

In general, with such a system it is easy to organize medical service for all segments of the public, since those paying for the insurance, who have signed an economic agreement for medical service, may be different government, public, and private structures. At the same time, the presence of a mobile third part of the budget prompts competition between the government establishments for the contingent of the public being served.

In order for such an economic mechanism to actively function, it is necessary that all therapeutic prophylactic establishments (from rural to republic) be determined by ownership (government, collective, and private). It is a paradox, but true nonetheless: Until now medical establishments have not been legal entities. In the break-up of the government I foresee great structural changes in today's public health service. It is the abolition of hierarchal management structures and the transfer of functions for regulating the activity of therapeutic establishments in the conduct of the local Soviets, and the release from subordination to the Ministry of Public Health system. The bed network will immediately be reduced, if there is no need for them to have so many beds within the territory of the Soviet. Staffs will also be reduced.

Only registered medical establishments will be able to sign various agreements and contracts with insurance

organizations, legal enterprises, and people. Such a transition is appealing with its reality, and will make it possible to introduce elements of medical insurance and train the collectives of the medical establishments to work under the conditions of the new economic relations; each worker will realize that his work is of value, and the more effective he is, the more he will be valued, and thus the higher his salary will be.

### **Kazakh Health Minister on Syringe Production**

937C0107E Alma-Ata KAZAKHSTANSKAYA PRAVDA  
in Russian 29 Aug 92 p 5

[Article by Sergey Gorbunov: "General Purpose Disposable Syringe". First two paragraphs are KAZAKHSTANSKAYA PRAVDA introduction in boldface.]

[Text] In Kazakhstan today we not only have a shortage of drugs, but also of medical supplies. This includes disposable syringes. In a conversation with KAZAKHSTANSKAYA PRAVDA correspondent, V. N. Devyatko, Kazakhstan Minister of Public Health, said that they need 350-400 million disposable syringes annually to serve the public on a normal basis.

The medical establishments actually have much less than the actual number needed, and those that they do have are generally obtained on the side. It is true that the Pavlodar joint stock company Medpolimer has recently begun to manufacture disposable syringes. But its capacity is currently only 25 million syringes per year. There are no related plants in Kazakhstan, and the opening of any in the coming months is not anticipated.

It is not chance, therefore, that while in Pavlodar at a presentation of the Medpolimer joint stock company that V. N. Devyatko called the issue of the first Kazakhstan disposable syringe a historical event, an event symbolizing the birth of the medical industry in Kazakhstan.

I do not think that the minister is exaggerating. The joint stock company Medpolimer was at first created as a joint government-cooperative enterprise born of the enthusiasm of several energetic and enterprising people. The point is that when under the old guard a boom sounded for disposable syringes, Pavlodar (like other cities in Kazakhstan) was not on the list of regions outlined for the location of a "syringe factory". And that is when the enthusiasts, G. Nikiforov, former director of Medpolimer, M. Khurin, current president of the Union of Cooperatives and other enterprising agencies in Kazakhstan, and Sh. Kapkayev, general director of the Kustanay Textile Factory Kotex, addressed the Kazakhstan Council of Ministers. Thus there was a special resolution to establish in Pavlodar a plant for manufacturing disposable syringes.

I cannot describe in detail how "happy" the former directors of Pavlodar Oblast and the Kazakhstan Ministry of Finance were at the birth of the new semi-government plant. First, for a long time they could not



find a building site for it, and second, the financing was very slow in coming. Then, out of kindness the Kazakhstan Entrepreneurs Union gave 1.5 million rubles and the Kustanay Textile Workers gave 5 million. The Pavlodarenergo Production Association and Pavlodar Production Association "Main Pipelines" collectives made their contributions. These resources were used to begin construction of the first workshops and the creation of a design institute for the medical industry.

Then, with a new director at Medpolimer, S. Sultanov, they began to raise the capital buildings of the enterprise and renovate those purchased earlier.

"We knew," says Serik Yegelyevich, "what was needed, without waiting for the base production to begin, to form a collective, and raise the capital, otherwise we would not survive. At the site of the former establishment of the Ministry of Internal Affairs, to put it simply—zones, we equipped the workshops for producing lotion and toothpaste, here we began to cultivate mushrooms, manufacture plastic caps for medicine bottles, casings for ballpoint pens, and established a small venture for dressing rabbit furs and manufacturing wooden folk dishes and souvenirs. All of this is currently giving us a profit. But the main thing for us is the syringes. In order to accelerate their production, we signed an agreement with the Pavlodar Aluminum Plant. We are renting from them in the gallium workshop, where there is the required purity grade and production area. We set up equipment there with a capacity of 25 million syringes per year and have already produced 200,000. Naturally, this is a temporary solution. We need to finish construction of the main buildings.

"The framework of two buildings has already been erected on the construction site for the production of 70 million syringes and 25 million blood transfusion systems. Buildings for administrative services and the laboratory are rising. In the future we are planning the production of an artificial kidney and metal needles. The stockholders of Medpolimer, having produced the first-born of the medical industry in Kazakhstan, are already living in the future."

I asked S. Sultanov how much time would be necessary to get all this deficit production going.

"Everything in many ways depends on the government of Kazakhstan," he responded. "We have the equipment for manufacturing 70 million syringes. The Entrepreneurs Union has already purchased a sterilizer for disinfecting them (we are currently doing this in Uzbekistan). The stockholders are donating some of the money to finish construction of the first and second lines (syringes and blood transfusion system). Then we need government help. The first thing is to get us included in Australian and German credit lines. Then we will be able to obtain the necessary equipment for manufacturing systems and needles (incidentally, the Karmetkombinat, according to Sultanov, is ready to deliver a special metal for this, S. G.). And finally, we need help with the

finances to finish construction on the workshops. If we are met halfway, in 1.5 years we will be able to begin work.

"The perspective is alluring. And when you consider that similar factories being built in Stepnogorsk, southern Kazakhstan, and eastern Kazakhstan oblasts are still far from completion, it would make sense at this level to concentrate all our efforts to accelerate the start-up of all the capacities of Medpolimer. It could considerably help doctors until the other above-mentioned factories in other regions of Kazakhstan are put into operation. Therefore, it is just for this reason that the Kazakhstan Minister of Public Health promised to help Medpolimer—to present the respective proposals to the Cabinet of Ministers.

"It is good, if this is so. It is good if the government will also meet them halfway. The last thing I want to do is scare anybody, but there is very little good that you read nowadays about how in Russia and in other countries of the CIS there is a sharp increase in AIDS cases and that of 100 infected persons, 80 have already died, and the forecast is for a probable increase in infection and mortality. And even if this fate bypasses Kazakhstan for now, each time you are in a treatment room, you will somehow feel uncomfortable when you are pricked with a needle that has already been used to inject several other people."

#### **Production of Radioprotective Medicine Begins**

937C0107F Alma-Ata KAZAKHSTANSKAYA PRAVDA  
in Russian 29 Aug 92 p 5

[Article by Rashid Garipov: "Elixir Manufactured in Talgar". First paragraph is KAZAKHSTANSKAYA PRAVDA introduction in boldface.]

[Text] "VITA" is the name of the small plant created last year by L. S. Bekasov, a physician from Talgar. Its chief product is olevit, a product of sea buckthorn oil, and was developed by Leonid Semenovich.

The path to creating a new drug was long, hard, and dangerous. The inventor of the elixir had to not only study the formulas of Tibetan medicine and alter the formula based on modern research, but he also had to endure the persecution of various government agencies and was even subjected to judicial investigation. But it seems that today all this is in the past; the drug has found its way to the patients.

The point is that pharmacists of "VITA" were able to enhance the properties of the sea buckthorn oil. As a result the novel preparation neutralizes the products of the deleterious effect of radiation, toxic substances, nicotine, alcohol, and substances facilitating the growth of malignant tumors on the human body.

Olevit has a rather broad spectrum of use. It can be used as an anti-inflammatory agent in the treatment of gastrointestinal tract diseases, in surgery, and in gynecology.

The small plant is planning to export "VITA" abroad. After all, "abroad" a bottle of the curative elixir will cost 200-300 dollars, but here the preparation is available in pharmacies for 100 rubles per 100 grams.

### **Chimkent Pharmaceuticals Plant Cuts Staff**

937C0107G Alma-Ata KAZAKHSTANSKAYA PRAVDA in Russian 29 Aug 92 p 5

[Article by Nina Ishutina: "You Can't Afford Medicine?"]

[Text] Forty percent of the employees at the Chimkent Pharmaceuticals Plant were affected by an order to reduce the staff. The number includes 75 engineers and 120 laborers.

Kazakhstan's leading pharmaceuticals plant is in a critical situation. The demand for manufactures from the plant has fallen sharply due to the significant increase in price. The plant's storerooms are filled with unsold pharmaceuticals. The Chimkent Pharmaceuticals Plant had to cut production, which also affects the staff.

### **First Medical Institution Privatization in Kazakhstan**

937C0107H Alma-Ata KAZAKHSTANSKAYA PRAVDA in Russian 29 Aug 92 p 5

[Article by Bulat Yerezhepov: "Privatization in Medicine".]

[Text] The Kustanai Therapeutic Production Association of Mental Medicine has become a government joint stock company. This is the first therapeutic establishment in the oblast that has dared to take such a step. We know that privatization of medical establishments in the republic is barred. But the Kustanai Territorial Committee on State Property decided to invoke the presidential edict, which gives committees autonomy in selecting their objects of privatization. The collective of the association solidly set about reformation. The resolution on making the establishment a joint-stock company was adopted almost unanimously at the founding conference. The famous psychotherapist A. L. Katkov was elected president of the joint-stock council.

### **Draft Health Insurance Legislation**

937C0107I Moscow MOSKOVSKIYE NOVOSTI in Russian 9 Aug 92 p 2

[Article by Yekaterina Glebova: "How Much Does the Bulletin Cost". First paragraph is MOSKOVSKIYE NOVOSTI introduction in boldface.]

[Text] The Moscow government decided to replace the free public health service that everyone was accustomed

to with health insurance. The plan is being polished up, but the opportunity has arisen to discuss in more detail that which frightened us for many years.

### **The Exceptions Health insurance should enter each Moscow residence 1 January 1993.**

For a rather broad category of unemployed citizens—children, retirees, and the disabled—nothing has changed. They will continue to be treated as in the past, without even thinking about the sums that will be paid for them by the municipal budget. The municipal budget will also finance intermediate care in emergencies, "first aid". In addition, the government budget will pay for the treatment of infectious diseases.

### **The Rule Treatment of everything and everyone not covered by the exceptions will be according to the following system.**

The employer (plant, private enterprise, budget establishment) will pay a given amount to the public health municipal fund) for each of its employees. Then the Chief Medical Directorate will select and credit from among the available insurance companies the one in their opinion that is most worthy, and will give them the right to collect dues, distribute territories, etc. At that moment, when going to the polyclinic it will be enough to carry an insurance policy from one of the companies. The polyclinic will register it, record particulars of the company, and at the end of treatment will send a bill. It is believed that treatment for one person will cost the employer 3,000 rubles per year. However, taking into account paying for the activity of the insurance company, its staff, and the insurance policy forms, the sum will quite tangibly increase. In addition, there will be indexing in the fourth quarter. The employer gets the money from its own labors. But taking any "treatment" amounts from the employees' salary is prohibited.

### **The Initiative**

The elements of the other, voluntary insurance are already in place. Better medical service is more expensive. It is paid for either by the employer or the patient himself. Then, depending on the amount, you can even be treated in the Kremlin polyclinic or at the Fourth Directorate of the Ministry of Health, which is what many successful businessmen do.

The director of the Moscow Chief Medical Directorate, Anatoliy Solovyev, informed the MOSKOVSKIYE NOVOSTI correspondent that no constructive changes in this program are foreseen and on 25 August it will again be presented to the city government.

**Role of Periodic Press in Illuminating the Medical and Social Aftereffects of the Accident at Chernobyl**

937C0111A Minsk ZDRAVOOKHRANENIYE  
BELORUSSII in Russian No 10, Oct 92 (manuscript  
submitted 29 Apr 92) pp 55-57

[Article by Yu. T. Sharabchiyev, N. V. Bazulko, Ye. V. Shokavina, Republic Department of Scientific Medicine and Medical-Technical Information, Ministry of Health, Republic of Belarus; UDC 614.73:002(07)]

[Text] Concerns among the populace about the adverse effects of the environment on the individual and his mental and emotional state largely depend on the nature of the coverage of a given situation by the mass media.

It is recognized that the extent of people's knowledge of biomedicine and hygiene has an important impact on their health state. The experience gained in several countries gives evidence that the specific promotion of healthy lifestyle (well-balanced diet, physical exercise, observance of hygiene rules, quitting smoking and alcohol abuse, etc.) produces a real increase in average life span and a decrease in the morbidity rate.

All of the above is extremely important for Belarus, which has suffered substantially from the Chernobyl accident, because additional factors that influenced the morbidity structure of the population residing in the contaminated areas included not only the effects of ionizing irradiation and radionuclides in food products, but also a high level of radiophobia. The major cause of radiophobia is the lack of general knowledge of radiobiology among the population and the lack of it in popular-science literature explicating the problems of radiation medicine and hygiene in an understandable form, as well as the dissemination by different sources, including the press, of incorrect information. A sociological poll taken by the newspaper GOMELSKAYA PRAYDA showed that 53.6 percent of the respondents living in the city of Gomel agreed completely with the opinion that the radiological situation in the city is very dangerous, whereas 29 percent agreed to a large extent; 81 percent of the respondents noted they felt worse; 58.7 percent expressed their desire to leave the city; and 30.6 percent of medical workers pointed to the lack of radiation-medicine knowledge. As a result of that, the job of the mass media must include specific work to eliminate mental and social tension and elevate people's knowledge of radiological issues, which would help the development of a healthy lifestyle, good work habits, proper diet, and better survival rates among the population in areas with elevated radioactivity.<sup>1, 2, 3, 4</sup>

Our objective was to study the level and nature of the coverage of the problem of the elimination of the aftereffects of the Chernobyl accident in the mass media. To do this, we analyzed 842 articles from 104 newspapers and sociopolitical journals published in countries of the CIS in 1991. In the analysis, it turned out that more than 2/3 (578) of all the articles of interest to us had been

published by 16 newspapers and the remaining 1/3 of newspaper and journal articles had been carried by 88 mass media organs.

In Belarus, the problem of eliminating the aftereffects of the accident was discussed most frequently by the newspapers SOVETSKAYA BELORUSSIYA (80 articles), ZVYAZDA (66), VECHERNIY MINSK (42), and GOMELSKAYA PRAYDA (36). In Ukraine, that problem was most frequently addressed by the newspapers RABOCHAYA GAZETA (33 articles) and PRAVDA UKRAINY (16). In Russia, the Chernobyl accident was more often discussed by the central newspapers PRAVDA (43 articles) and TRUD (36).

The study of the coverage on the pages of newspapers and social-popular journals shows that the largest number of articles were published in Belarus (63.8 percent) and that few were published in Ukraine (6.9 percent), Russia (27.9 percent) and other republics of the CIS (1.3 percent). Among newspapers and journals of Belarus the greatest number of articles devoted to the problem appeared in the republic-level press (39.4 percent) and in local publications from the oblasts with the highest levels of contamination with radionuclides (Gomel Oblast, 14.5 percent and Mogilev Oblast, 3.4 percent).

When analyzing the content of the above publications, we singled out major topics they addressed. It turned out that social (530 articles) and political (513) aspects were distinctly predominant in the publications dedicated to the Chernobyl accident. Significantly less attention was given to medical (387) and environmental (302) issues associated with the elimination of the aftereffects of the accident, in spite of the fact that these problems play the crucial role in providing normal conditions for the life and survival of the people in radionuclide-contaminated regions. Still less attention was paid to scientific and technical aspects of the elimination of the aftereffects of the accident, although they strongly affect the fundamental solution of the problem of accelerated elimination of radionuclides. No matter how strange it may be, the most unpopular topics in mass media were problems of every-day life (114 articles) and hygiene (2).

The examination of publication distribution in terms of regions and problems showed that political issues were most actively discussed by republic newspapers and journals of Belarus, as well as the central newspapers of Russia. In local publications of the oblasts with the greatest contamination, the political problems were elucidated to a much lesser extent, with primary emphasis given to environmental and medical aspects that reflect the every-day concerns of the local population.

A more detailed examination of the topics associated with the elimination of the aftereffects of the Chernobyl accident as covered by mass media demonstrated that they can be categorized in the following manner. The highest number of articles deals with international aid (161), followed by children's illness and treatment (132),

criticism of health care organs (131), dosimetric data for various areas (123), therapy for the accident victims (114), problems facing resettled residents (97), morbidity rate in the irradiated areas (94), legal aspects (83), food monitoring (76), etc. Among the themes we identified, only a few (treatment, prophylaxis, legal aspects, and a few others) could be of real help to the population, but the percentage of them in the total number of articles was extremely low. Our analysis of the articles showed that international aid was discussed primarily by the republic-level press of Belarus and the central press of Russia. These same publications give more attention to care given to children and criticism of administrative organs. In the radionuclide-contaminated areas, the mass media pay more attention to practical issues: dosimetric control, resettlement, food monitoring.

An examination of article distribution in the mass media with respect to categories of authors demonstrated that most of the articles had been prepared by professional journalists, whereas representatives of social organizations had authored only 37, and laymen, 61 publications. Of highest priority for journalists were the following issues: international aid (129 articles), children and radiation (87), and criticism of administrative organs (79).

Of greatest importance for scientists—medical workers included—were problems associated with dosimetric control data (62), food monitoring (43), morbidity rate (30), and therapy (28) in the radionuclide-contaminated areas.

Staff members of administrative bodies, in their articles, most frequently discussed regulatory and legal issues (45), organizational aspects of the elimination of the aftereffects of the accident (32), activities of administrative bodies (28), and international aid (20). Staff members of social organizations wrote primarily about activities of their organizations (15) and international aid (15).

Laymen mainly criticized administrative organs (22), discussed every-day-life problems (15), and resettlement issues (15).

We investigated the content of the article texts by applying the method of cluster analysis of key words, which consists essentially in identifying the relationship among descriptors reflecting the sense of a document. After first establishing a threshold of concomitant occurrence of descriptors in text at 20, we then formulated a cluster of interactive problems involved in the elimination of Chernobyl accident aftereffects. This cluster included two main subject areas: medical aspects of eliminating accident aftereffects (described by six descriptors) and every-day-life and resettlement problems (four descriptors). The area of legal aspects was represented by one descriptor, and the area of radiation ecology, by two descriptors. An isolated cluster consisting of two descriptors dealt with cleanup personnel. The central nucleus of the cluster was a descriptor:

"Criticism of administration bodies," which combined the rest of the problem areas of the cluster.

Thus, our analysis of articles in the mass media devoted to the elimination of the aftereffects of the Chernobyl accident revealed crucial shortcomings which should be taken into consideration in future work.

### Conclusions

1. Articles in the periodic press about the Chernobyl accident are politicized; they are frequently accusatory and not constructive; they are often overemotional and sensational and aimed at protecting departmental interests, and they ignore the potential responses of the reader.
2. The mass media have inadequately promoted scientifically documented healthy lifestyles among the residents of contaminated areas. Published data are often fragmentary, have a weak sociological foundation, and lead to an increase in mental and emotional tension rather than to its decrease.

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### Pokrovskiy on Objectives of Russian Medical Academy

937C0138A Moscow VESTNIK ROSSIYSKOY AKADEMII MEDITSINSKIKH NAUK in Russian  
No 6, Jun 92 (signed to press 31 Jul 92) pp 5-11

[Article by V. I. Pokrovskiy, academician of RAMN, president of the Russian Academy of Medical Sciences, under the rubric "First (64th) Session of the General Meeting of the Russian Academy of Medical Sciences, 24-25 March 1992": "Tasks for the Russian Academy of Medical Sciences To Further Develop Medical Science"; UDC 61:008(470)]

[Text] By ukase of B. N. Yeltsin, president of the Russian Federation, dated 1 January 1992, the USSR AMN [Academy of Medical Sciences] was changed to the Russian Academy of Medical Sciences (RAMN). At first glance, it would seem that this is merely a change in

label. In fact, the ukase must inaugurate a new stage in development of medical science in our country. The status of self-managed higher scientific medical organization of the Russian Federation not only grants the Academy broad rights, but also imposes a great responsibility for the level of research carried out in scientific research institutes of the Academy, the nation's VUZ's [institutions of higher learning], institutes and institutions of the Ministry of Health of the Russian Federation, Committee for Sanitary and Epidemiological Oversight, institutions of clinical health care, institutions of other ministries and agencies.

It must be borne in mind that the catastrophic situation with respect to financing of science, the personnel question (drain of personnel within and outside the country), progressive lag of material and technical support of research, dramatic decline among young people in the prestige of a scientist and other circumstances have created enormous objective difficulties in implementing the ukase.

At the same time, the adverse trends in health status of the Russian people, which have been particularly exposed in recent years, require the utmost attention.

Among the end indicators of health, as we know population growth indicators are in first place, and they are in a dangerous condition. Natural population growth dropped from 8.1/1000 population in 1965 to 4.9 in 1980 and 0.7 in 1991, i.e., there are signs of decrease in population size. The dramatic deterioration of standard of living, uncertainty of most people about the future with the change to a market economy have been manifested, first of all, by a decline of birthrate from 15.9 in 1980 to 12.1 in 1991, which is unprecedented in peacetime, and corresponding rise in mortality from 11.0 to 11.4/1000 population.

There has been a consistent increase in number of abortions which, as we know, have an adverse effect on female reproductive function. In 1990, it was twice the number of births. Mortality rate is rising more intensively in the age group over 30 years. A comparison of standardized indicators of overall mortality rate among able-bodied men revealed that the same indicator is almost twice the level in developed countries, for women it is 1.5 times higher; mortality due to circulatory diseases is twice as high among both men and women, that due to accidents is 2.3 times higher for men and 1.5 times higher for women; for respiratory diseases it is almost three times higher for men and 1.6 times higher for women.

The foundations for good health are laid in the earliest periods of life, and for this reason problems of mother and child health care should, as before, hold a priority status in the research programs of the Academy.

At the present time, a team of scientists has completed an investigation entitled "Status, Trends and Forecast of Infant Health in the Russian Federation," which was forwarded into the system of the president of the Russian

Federation. The facts submitted there indicate that the health of women in Russia, including pregnant women, merits serious attention. A total of 75.1 percent of the women of childbearing age have some health problem. The share of healthy infants in the neonate population dropped from 48.3 to 36.5 percent; there has been a 1.4-fold rise in share of neonates with congenital disease or chronic pathology acquired in the perinatal period.

Thus, the current demographic situation in Russia, like the health status of the growing generation, can be viewed as critical. Since all these processes are static, there is no reason to expect an improvement in the situation before the year 2015. For this reason, the immediate task for the Academy is to elaborate long-term strategies for safeguarding the people of the Russian Federation, and speedy restoration of their health. At the present time, a large team of scientists in different specialties is completing preparation of a report to the president of the Russian Federation on "Health Status of the People of the Russian Federation," in which the health status of the Russian people will be assessed as related to regional, national and occupational distinctions. Apparently, the next session of the general meeting of the Academy should deal with the results of this investigation, and priorities of research programs and directions should be defined.

It is also imperative to elaborate without delay a program for social development of protection of mothers and infants in the period of transition to a market economy and subsequent years, bearing in mind that the introduction of medical insurance could lead to appreciable reduction of preventive, diagnostic, and therapeutic programs, which would lead to further worsening of the situation.

But basic research remains as the main task for the Academy. Problem-targeted programs aimed at solving the most important problems of health care should be formed on the basis of the new data obtained from such research.

The Academy must strive to investigate man in all the diversity of his activities. On the basis of proposals of 42 scientific councils of the AMN of the former USSR, the research-coordinating board of the Academy presidium has developed the basic directions of research in the Russian Federation for 1992-1995, which should be discussed at a session of the general meeting of the Academy.

When the AMN of the former USSR was organized in 1944, I. V. Davydovskiy stated that the main guideline should be synthetic, problem-oriented and topical approaches to solving the problems put to the Academy. One could hardly object to this thesis today.

As we know the USSR AMN was founded in the most difficult times. Probably not all those present and even Academy members know that the idea of organizing the AMN, judging from existing documents, had been discussed even before the war in 1941. It arose because



everyone realized clearly that the VIEM [All-Union Institute of Experimental Medicine], which was the main center of theoretical medicine in which the best minds of that time were concentrated, had little connection to clinical practice and no contact with the main problem-oriented institutes, and for this reason could not affect coordination and planning of medical science on a national scale. But in those prewar times, it was decided to wait a little with establishment of the Academy. Then the war struck, during which there was even more acute realization of the need to unite theoretical and clinical medicine, all research carried out in medicine, into a single complex, to organize distinct coordination of research conducted in the nation.

On 3, 9 and 15 June 1943, at sessions of the Scientific Medical Council of the USSR Narkomzdrav [People's Commissariat of Public Health], there was discussion of a draft of a paper by N. N. Burdenko, which was then forwarded to the government. While the question of desirability of organizing the Academy of Medical Knowledge (which is the name more often used for the future academy) raised no questions, the structure of the academy and the main tasks put to it were the subject of comprehensive discussion. It is remarkable that the subject of discussion was extremely close to the present one: should the Academy have its own bases (institutes), or would it be only an ideological superstructure, and advisory body on the order of the Scientific Medical Council of the Narkomzdrav, and should all Narkomzdrav institutes be transferred to the Academy or only some of the large prominent ones, whose work was of basic importance? N. N. Burdenko believed that one should create surgical, therapeutic and other combines (centers) pursuing clinical and theoretical work to equal degrees. I. V. Davydovskiy stressed, "It is not a disciplinary, but primarily a problem-oriented approach" that is required of the Academy structure. L. A. Orbeli believed that the main task for the Academy was to plan research in the entire country, as well as train talented scientists, since an outstanding personality is the main moving force in progress of science.

The USSR AMN was founded. The first session of the general meeting of the USSR AMN convened in Moscow on 14 December 1944.

As you see, the Academy was born in just as difficult times for the nation. However, large subsidies were allocated for equipping institutes, the Akademstroy [Academy committee for construction] was organized, the Academy research base was deployed, and much was undertaken to improve appreciably the financial situation of all ranks of research workers. All this enabled the Academy to become an extremely large world center of medical science within a relatively short time, and allowed Academy scientists to make a substantial contribution to its development.

In 1944, the Academy comprised 25 research institutes, and in early March 1992 there were 64 (including 25 institutes within research centers). They are manned by

8286 scientific associates, including 1225 doctors and 4484 candidates of sciences. Nineteen institutes situated in CIS nations have been singled out of the Academy. At the present, the Academy has 334 members, including 152 active and 182 corresponding members, as well as 28 foreign members. Among Academy members, 54 live and work in CIS nations (other than Russia).

All former members of the USSR AMN confirmed their agreement to become RAMN members.

The conversion of the USSR AMN into the independent RAMN raised its status and made it necessary to define the basic guidelines for Academy activities.

Under the new economic and social conditions in the Russian Federation, the priority organizational tasks for the Academy are: to elaborate the basic directions of development of medical science in accordance with the needs to protect the health of the public; implement coordination of research carried out by research centers, scientific research institutes, medical VUZ's, and other organizations of Russia; implement a unified complex system of planning, coordination, expert evaluation, financing and control of execution of research; training scientific personnel with the highest qualifications.

The Academy must persistently implement further democratization of activities of scientific research institutes, devote more attention to providing the necessary conditions for creative work of authors of original ideas and innovations, regardless of their place of work, and in so doing to decisively combat pseudoscience which is so widespread in our days.

The scientific research institution is the main organizational structure of the Academy. It is imperative to further broaden the rights of institutions that must solve most problems, including financial ones, independently. We must elevate the role of scientific councils in institutes and, as shown by experience, by no means replace them with councils of employee groups. In the latter case, the competence of a specialist is replaced with a narrow-minded principle: what is most advantageous for me. It is necessary to hold broader and more frequent discussions of the basic medical problems. The Academy presidium should elevate the role of scientific councils and problem commissions, not only assigning duties to them, but also granting them specific rights, in particular those pertaining to distribution of funds for research in terms of grants.

In this regard, there should be speedy revision and confirmation in May-June 1992 of new members of scientific councils and problems commissions, with participation of prominent specialists from different regions and agencies of the land, including young talented scientists who have made a name for themselves in a particular field. It is necessary to elaborate the basic guidelines for organization of scientific medical research in the Russian Federation under conditions of a market economy. The Academy presidium, under the leadership of Vice-President F. I. Komarov, is working actively on



this matter. It is time to create a competent commission and instruct it to finalize the draft, so that it can be submitted for discussion at a general meeting of the Academy (no later than February-March 1993).

As we know, there are two directions of development of medical research centers in the world: 1) establishment of research centers as part of universities; 2) establishment of independent research sections. Both variants have advantages and disadvantages. Historically the second route was followed in our country. At first, research did not require the complex equipment that exists today, VUZ departments were able to maintain an adequate methodological level of research; at present this is more difficult.

At the same time, the VUZ's had a greater opportunity to select talented young people for employment and to offer broader professional training. It is now time to combine these opportunities. Some of the research institutes should probably be made part of medical institutes and universities, and departments should be given broader opportunities to use the material and technical potential of Academy research institutions. It should be stated that there are already various forms of interaction between VUZ's and research institutes. However, they are formed exclusively on the basis of personal initiative. It is necessary to investigate existing experience and integrate more intensively VUZ and Academy science, which would permit more intensive use of the strong scientific potential of VUZ's. Evidently, one of the vice-presidents should head this work, and a special group should be formed within the structure of the Academy presidium.

It is planned to expand the authority of the office of institution departments, both specialized research and regional ones, in order to further democratize the work of the Academy. In 13 years, the Siberian Department of the Academy, which was organized in 1979 at the Siberian Affiliate, has become a major research center in the eastern part of our country. Ten new scientific research institutes were opened. In 1987, the East Siberian Affiliate in Irkutsk, departments of foreign languages and philosophy were organized, and the SKB [special design office] created the specialized Medbiofiz-pribor [biomedical and physical instrument] section.

The scientists in the Academy's Siberian Department have carried out some research developments that are relevant to theoretical and clinical medicine. A previously unknown phenomenon in immunology—erythroid cell regulation of humoral immunity—was recorded as a discovery. Basic research has been completed in the psychophilic nature of a number of pathogenic microorganisms. Some new methods of diagnosing, preventing and treating pseudotuberculosis have been developed and adopted in clinical practice. New data have been obtained on biochemical and immunological bases of human vital functions under the conditions of Siberia, the Far East, and Extreme North about the clinical

aspects and pathogenetic mechanisms of human adaptation to these environmental and climatic conditions, with due consideration of social and industrial factors; recommendations have been elaborated for optimizing living conditions for man in different eastern parts of the country, etc. Regional distinctions have been found in symptomatology, pathogenesis and incidence of diseases most frequently encountered in Siberia.

As you see, the regional principle of development and organization of medicine has been justified. The Academy presidium deems it necessary to examine further the desirability of opening Academy departments and affiliates in a number of regions (Far East, St. Petersburg and others), as well of attaching the Tomsk Research Center to the Siberian Department.

It is imperative to give comprehensive consideration and to discuss further steps for preservation and strengthening of existing scientific ties with scientists of CIS nations, basing this work on broad circles of the medical community, in particular, when creating various associations, funds and comprehensive programs of research. The mutual activities of RAMN and RAN require strengthening and specification. In spite of the repeated decisions of the USSR AN and USSR AMN concerning stronger interaction aimed at working on basic and applied health-care problems, they still cannot be deemed satisfactory. The "Basic Sciences To Serve Medicine" (1980) program has been left virtually untouched, in spite of the fact that it outlined specific development of new medical drugs, and new types of medical technology. RAMN ties with other academies are also inadequate.

Financing is of paramount importance to future development of the scientific potential to the front lines. As we know, in the former USSR, medicine was in next to the last place among the 34 basic sections of national science with regard to volume of financing. Under the 11th Five-Year Plan, mean annual cost of basic funds for all scientific institutes, medical VUZ's and institutes for advanced training of physicians increased by only 190.2 million rubles, while mean annual growth was only 1.3 percent.

At the same time, there was many-fold increase in allocations in the civilized world (as western nations are now called) with increase in complexity of methods of studying man as a biological object. In developed countries, financing of medical science in many priority directions increased by 20-30 and more times in 5-6 years. This resulted in a number of outstanding achievements.

Expenses for science in Academy institutions constituted 324,793,000 rubles in 1991. About 170,000 of this amount constituted basic financing, 70 million for the GKNT [State Committee for Science and Technology] program "Control of the Most Widespread Diseases," about 57,000 for the "Chernobyl" program, 8000 for other programs ("Human Genome," "Genetic Engineering," and others), 15,000 made up the centralized fund of the Ministry of Health, and 4,500,000—the VKNTs

[All-Union Cardiological Research Center] fund, concurrently from the president's reserve fund. The Siberian Department spent 35,100 rubles.

The AMN announced a basic budget of 1,149 million rubles for 1992 (the Ministry of Science allocated about 680 million rubles); 172 million rubles for the program "Control of the Most Widespread Diseases," 60 million rubles for the "Chernobyl" program, 216 million rubles for the Siberian Department (130 million allocated). In all, 809.5 million rubles were allocated.

Only control figures for basic financing of RAMN research in 1992 were examined by the Ministry of Science.

The allocations for the first quarter of 1992 were defined according to status as of 21 March 1992, with a growth index of 3 in relation to base 1991 allocations. This included a 1.9 wage hike but was underestimated by 1.45 times, as ensues from the government's decree.

The national scientific and technical programs, "Control of the Most Widespread Diseases" and "Human Genome" will be financed directly through the head organizations, bypassing the finance administration of the Academy. Thus far, the "Chernobyl" program has received no financing in 1992.

The serious financial situation in our country automatically affected capital construction. For example, the prices for construction work and services increased by about 40 times. A total of 69.4 million rubles was allocated for the first quarter of 1992. There has been virtual destruction of the previously operating mechanism of material and technical support of construction projects, with respect to materials and equipment. An effort was made, in accordance with the decision of the government of Moscow dated 20 Aug 91, to auction off unfinished structures for a nutrition building and scientific research institute of psychiatry and rheumatology. At the present time, a similar question is being raised about the unfinished building for the Scientific Research Institute of Neurosurgery imeni N. N. Burdenko. This is in spite of the fact that the building of this institute is falling down, while the Institute of Resuscitation has no reliable roof over its head.

There have been no requests for the considerable volume of research and planning work for the future construction of Academy facilities (endocrinology, occupational pathology, pediatrics, pediatric oncology, pharmacology and others).

A particularly difficult situation is developing for the clinics of Academy institutes, the bed resources of which constituted 7564 as of 1 January 1992 (2035 in the Siberian Department). It should be borne in mind that most clinics are unique to the Russian Federation; they have a concentration of personnel; they are outfitted with modern equipment to some degree or other; complicated operations are performed there; the latest and most sophisticated investigative methods are used. But

they are virtually without financing. The Academy budget for upkeep of clinics has still not been examined by the Ministry of Finance, and no control figures were defined for this year.

The 2.7-fold increase in financing in the first quarter of 1992, as compared to the same period last year, turned out to be overtly inadequate, since the expenses for institute upkeep under prevailing prices increased by an average of 10-15 times. For example, the Institute of Surgery imeni A. V. Vishnevskiy was issued a budget allocation of 9.5 million rubles for the first quarter of 1992, which corresponds to 40 percent of the minimal requirements.

If we extrapolate the level of allocations for the first quarter of 1992 to future periods, we can project that 50 percent of the allocated sum will have to be used for wages, in accordance with the minimum salaries and wage schedules spelled out in government decrees, ukases and orders of the Russian president, which are government guarantees for preserving the minimum wage.

There was a 10 to 15-fold increase in material expenditures. Transport expenses increased by an average of eight times, the prices of medical equipment and spare parts—by 10 times, and there was a 15-fold increase in expenses for raw materials, supplies, major repair, etc.

The absence of governmental fund distribution and change to supply on the basis of direct contracts with suppliers have led to a dramatic increase in expenses for nutrition and drugs.

The question of compensation for the nutrition of hospitalized patients has not been resolved to this day, and even the tentative standard per bed-day has not been set. The average expense for nutrition increased by 8 times and constitutes 25-30 rubles per day, although at least 50 rubles per day per patient are needed to provide a standard level of consumption at the prevailing prices.

The previously projected 4-fold increase in drug prices has not been obtained to this day. Along with financial difficulties, there is instability that is related to absence of guaranteed deliveries. At present, no tendency toward improvement of the situation is seen.

Thus, the institute clinics, in which highly qualified care is administered to the residents of the Russian Federation are experiencing objective difficulties in maintaining the minimum level of the treatment process and performance of complex and unique operations conforming to worldwide standards and requiring major material and financial expenditures. If the system of financing and guaranteed supply of drugs, preparations, surgical instruments, suturing material, etc., is not changed in the near future, it would lead to a reduction and, in a number of cases, total absence of medical care, including surgical interventions. As a result, there could

be a decline in level of rendering highly qualified medical care and loss of leading positions by our science and clinical practice.

There is a real question of eliminating several of the most important laboratories (microbiology, radioisotope, physiology) and reduction by one-third in staff of clinical departments within the next 2-3 months.

The public cannot grasp the idea that medical care is becoming a paid commodity in our country. This is not a whim of scientists and physicians, it is a real necessity resulting from the economic policy. And we, physicians and scientists, should tell the public openly that it is impossible to render qualified medical care on the funds allocated by the government for health care. For this reason, if financing is not provided, we are faced with a choice: qualified care must become a paid service, or else it must be dramatically limited.

In accordance with the order of the Ministry of Economics and Finances of the Russian Federation dated 6 February 1992, in 1992 funds will be allocated on a monthly basis in minimal amounts: expenses for wages, bonuses, grants, pensions, nutrition, acquisition of drugs, heat and lighting, communications and rental of facilities totaling 100 percent of the month's allocations. The rest of the expenses can be financed if there is a surplus in the income part of the republic budget, i.e., no funds are provided for research as such.

Allocations for the month following the reporting one will be made only to the extent of spending budgeted funds in accordance with submitted monthly reports about actually spent funds. Thus, there cannot even be a question of purchasing any expensive equipment.

Due to the lack of funds, the Ministry of Finance did not allocate funds for other expenses in the first quarter of 1992.

In 1990, planned hard currency in the sum of 3 million rubles was allocated to scientific research institutions of the Academy, and 3 million rubles in hard currency for the AIDS problem. Contracts were signed for a total of 5,548,000 rubles; 2,576,000 rubles were received and 1,753,000 paid.

Commercial firms demand payment or return of equipment that is already in use. The USSR Ministry of Health provided in the 1991 import plant 1.6 million rubles in hard currency for the purchase of spare parts and expendable supplies, but this sum was reduced to 700,000. Contracts have also not been paid. The institute incomes from scientific research carried out on a contractual basis is not large: 26 million rubles as of 1 January 1992, versus 9 million in 1991.

The Academy presidium has no reliable data concerning other income in the institute budget.

In view of the significant rise in wholesale prices for medical technology and items for technical purposes, there have been more frequent cases when scientific

research institutions have refused to obtain it. For example, all four laboratory animal vivariums and the research laboratory of experimental biological models are on the verge of a disaster. The research institutes are not fulfilling their contractual obligations due to the lack of funds. For this reason, the cost of animals is rising. The existing situation could lead to a change in specialization of vivariums. It would require 10-15 years to restore their operation in the future. The knowhow gained in such work and trained personnel will be lost, and bear in mind that more than 15 million rubles in hard currency was spent in recent years to develop laboratory animal farming. The extent of readiness of the complex of buildings constitutes 70-80 percent; another 40-60 million rubles is needed to complete them, but the Academy does not have the money. Thus far, there has been no answer from the government to the application for funds.

In spite of the financial difficulties and sharp hike in travel and hotel expenses, the Academy must continue work on maintaining and developing international collaboration, which has thus far been characterized by a diversity of forms and directions. They include interacademy collaboration, intergovernment and interindustry agreements, participation in WHO work, interinstitute ties, and others. There are the most diverse ways of collaborating: joint research, exchange of specialists and lecturers, offering consultant aid, participation in congresses and meetings, exchange of information, and others.

In the 20 institutions there are 333 staff members who are collaborating with the center's WHO, and 11 plans are being implemented. In 1991, more than 900 Academy specialists participated in international measures. In 1992, it will be necessary to reduce the international ties for obvious reasons. However, with the change in Academy status, there is increase in volume of duties for members of the international administration, for which reason it will have to be reorganized.

For the same financial reasons, things are very bad in the area of publishing, particularly periodical publications. There are no funds to publish most periodicals, and if they do not get financial support they will either cease to exist, or their size and frequency will be reduced, and furthermore the prices will be raised and payment for publication will be instituted. As we have already stated at the beginning of this report, at one time the USSR AMN had its own publishing house. It is high time to restore it as a competitor with Meditsina [publishing house].

It is unlikely that the publishing problem could be solved in today's session. The only decision that the session of the general meeting of the Academy can make is to reduce by 0.5-1 percent the already meager budget of institutes, transmitting the funds to support periodicals.

It is apparent from the foregoing that the scientific research institutions of the Academy will be operating

considerably below the poverty level in 1992 and, probably, 1993, since one can hardly count on a serious increase in the national budget. Nevertheless, the Academy presidium deems one of its main tasks is to obtain a budget increase.

What then is the solution to the existing situation?

Conversion of the USSR AMN to the independent RAMN requires appreciable alteration in the system of organization and coordination of research. In particular, taking advantage of the presence of B. G. Saltykov, we insist that allocations to the RAMN fund be made from the basic science fund of MNVShTP [expansion unknown].

The system of organizing research in medicine used before in the former USSR provided for separate formation of plans for scientific research and their budgetary support.

Expertise and coordination of research were delegated to public scientific structures of the Academy (scientific councils of the USSR AMN and their problem commissions), while institute financing was implemented by the USSR Ministry of Health without consideration of their recommendations based on the surplus principle.

The actual processes of coordinating research and financing it were independent, having absolutely no effect on one another.

Progressive forms of organization, expertise and financing of research programs such as "Control of the Most Widespread Diseases," failed to find applications beyond such programs. That program virtually refined a grant system of distributing financial resources. What does it offer? Judge for yourselves: only 67 (34.5 percent) out of 194 applications pertaining to the AIDS program and submitted at the competition in 1991 were recommended for financing. Consequently, their executors will not receive additional funds for wages, purchase of equipment and reagents. This is why the Academy presidium believes that, at the present stage of development of medical science, it is imperative to devote special attention to providing conditions for the work of small research groups (teams) and individual researchers. This will reveal the most talented and promising ones, while the rest will have to shut down their activities. Thus, the institutes will rid themselves of a balance [sic] and reduce the number of personnel by at least 20-30 percent.

Expansion of target-oriented program planning requires enhancement of the role of expert evaluation of planned research and obtained results.

At the present time information data bases are being formed at the NKO [Research Planning Department] pertaining to expert evaluations, scientific plans and developments submitted for expert evaluation, competitions held, as well as computer programs to support expertise and mathematical processing of expert opinions.

The data bank pertaining to experts is a flexible structure that permits selection and recommendation of experts, formation of teams of experts for a specific program, which would limit monopolism, as well as access to developments and use of various programs as related to the purpose and nature of expert evaluation.

Even now, it is imperative for all ministries and agencies involved in medical research to prepare a coordinated statute on a unified procedure for organizing and financing scientific medical research in the Russian Federation. A draft has been prepared and is now under consideration. The RAMN must become the organizer, coordinator and expert in medical research.

Preservation of existing scientific and organizational structures with establishment of the mechanism for operation of the Academy under market economy conditions is the chief principle for utmost development of financing and management activities of the RAMN and its institutions.

Establishment of a financing and credit institution under the Academy could be the key element of such a mechanism. The Academy presidium has carried out a preliminary analysis of the feasibility of establishing such a department or the RAMN's own bank, and it asks the general meeting to voice opinions on this score. The bank could implement preferential services with respect to the financial operations of the Academy, institutes, enterprises and organizations collaborating with the Academy; it could pursue an investigative policy in the medical field and invest RAMN funds in other fields in order to develop Academy enterprises and organizations.

The Academy presidium, office of departments, administrators of scientific research institutes and VUZ's should develop scientific-production and commercial-entrepreneurial activities related to the sale of medical scientific and technical developments, patient treatment on a commercial basis, and cost-accounting projects. It is imperative to relieve scientific institutions, organizations and enterprises of RAMN of taxes, collections and duty fees, provided that the funds thus made available would be used to develop medical science, strengthen the therapeutic and scientific base of the Academy. Such proposals have been submitted in a draft of a government decree, which will probably be implemented in April of 1992.

Establishment of an RAMN Fund for financing original research by scientific teams and individual scientists is an important task for the presidium. On 22 January 1992, the RAMN presidium approved the decision to establish such a fund. At the present time it is undergoing legal formulation.



The fund is being established to aid in solving pressing problems in the area of medical research, to provide the necessary material-technical and financial conditions for practical implementation of scientific, social and charitable programs.

Citizens, worker groups, research and educational institutions, enterprises, institutions and public organizations of the Russian Federation, as well as foreign citizens and organization desiring to participate in the objectives of the Fund can be involved in its work.

The deteriorating socioeconomic situation in our country, increasing inflation, and dramatic rise in the cost of living have placed personnel of scientific research institutions in the medical sector in an extremely difficult and unequal position, as compared to workers in other sectors. All those attending this meeting are well aware of the fact that the average wages for personnel of research institutes is considerably below the minimal subsistence level. This is the chief cause of the drain of highly qualified personnel from the scientific field.

The coordination council for protection of the rights of scientific associates in the health professionals' union has addressed the government and Supreme Soviet of the Russian Federation with the demand for a five-fold increase in wages of employees of scientific research institutes, mandatory free medical insurance, and several other items.

The RAMN presidium supports these demands and believes that the session of the general meeting of RAMN will approve a decision to intensify social protection of medical workers. In view of the transition to a market economy and paid treatment, the RAMN presidium is searching for means of rendering free medical care to workers in the field of medical science, and starting in April 1992 dues will be raised to 950 rubles for active Academy membership and 475 rubles for corresponding membership.

In essence the Academy is starting in a new cycle of its development and activities since its organization in 1944. In comparing that period to the present, we should stress some of their basic differences. In the last 48 years, the Academy has undergone 2-3-fold "growth," and these years were marked with major scientific achievements. At the same time, it must be stressed that the catastrophic situation with respect to financing science, the personnel problem (drain within the nation and beyond its frontiers), total disintegration of the publishing field, the progressive lag in material and technical support of research, etc., in which the Academy finds itself today has not been experienced by medicine in the entire 48 years of the Academy's existence.

This is the reason for the objective difficulties in deploying research on the present, new stage of Academy development, since greater and responsible tasks have been put to it to coordinate and develop medical science on a national scale, and considerably more rights have been granted to do this. But implementation of these

rights is limited dramatically by the sorry state of the Academy, which we discussed above. Thus, we are faced with the discrepancy between the great responsibility and insufficient opportunities that exist objectively today to carry out the tasks put to the Academy.

The objective put to this first session of the Russian Academy of Medical Sciences is to find a way out of this situation and to at least preserve the scientific potential of medical science during the period of transition to a market economy.

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#### Decree of First Russian Medical Academy Session

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No 6, Jun 92 (signed to press 31 Jul 92) pp 11-14

[Article by V. I. Pokrovskiy, president of the Russian Academy of Medical Sciences, academician of the RAMN, and D. S. Sarkisov, chief scientific secretary of the RAMN presidium, academician of RAMN: "Decree of First (64th) Session of the General Meeting of the Russian Academy of Medical Sciences, 24-25 March 1992"]

[Text] In accordance with the ukaze No 5, dated 4 January 1992, of the president of the Russian Federation "Conversion of USSR Academy of Medical Sciences into the Russian Academy of Medical Sciences," the general meeting of the Russian Academy of Medical Sciences confirms its readiness to implement the functions imposed on the Academy concerning organization and coordination of medical science in the Russian Federation, determination and development of the most important directions of basic and applied medicine, and training highly qualified scientific personnel.

The general meeting of Russian Academy of Medical Sciences has identified the following basic directions of its work and tasks: implementation of general scientific supervision of research carried out by research centers, scientific research institutes, medical VUZ's and other scientific medical organizations of Russia; determination of a unified complex system for planning, coordinating, financing and management of research pursued in scientific institutions of the Academy and medical VUZ's; elaboration of social orders of the Ministry of Health and State Committee for Sanitary and Epidemiological Oversight of Russia, on a contractual basis; organization of independent expert evaluation of research, training scientific personnel with the highest qualifications, development of international scientific-technical collaboration.

Such priority directions of medicine and health care as forecasting the health status of the people in the Russian Federation, motherhood and childhood, strategy for individual and public health, medical genetics, immunology, biotechnology, biological mechanisms of human functions under normal and pathological conditions,



studies of different population groups, and others, require scientific investigation, theoretical validation and development.

The Russian Academy of Medical Sciences will continue to base its work on the scientific-sectorial and regional principle of organizing medical science, preserving and strengthening existing scientific ties with scientists and scientific institutions of the Commonwealth of Independent States and other countries, with support of its activities from broad circles of the medical community.

Restoration of the prestige of a competent scientist, value of scientific knowledge, professional training of a new generation of researchers, painstaking work with young people, screening and support of talented undergraduate and graduate students must become one of the most important prerequisites for development of medical science in Russia. They should be given the right of free choice of scientific supervisor, the right to individual interpretation of facts and theories, the right to independent scientific research.

The Academy must take all necessary steps to train highly qualified specialists, create material and research incentives for scientific associates, as well as sufficiently high wages and optimum research conditions in order to prevent the drain of talented specialists, particularly young ones, from the Academy system, offer the opportunity for scientific creativity, expression of scientific potential and innate talents. In order to solve the problem of training and retaining scientific personnel, the Russian Academy of Medical Sciences must combine its efforts with the resources of VUZ's, beginning with students still attending them. It is imperative to revive the glorious traditions of formation of scientific schools, to be concerned about the authority of scientists—administrators and educators—providing them with the opportunity of attracting on a broad scale talented people from different VUZ's of the Russian Federation. Under present difficult economic conditions, we must search for all means and various forms of financing medical science and enhancing the material and technical base of research. Great latitude for formation of research groups and teams of different sizes must be granted to the administrators of scientific research institutions, which are the main elements of the Russian Academy of Medical Sciences. Scientific institutions must have the needed independence of choice of direction of research and scientific topics, selection of personnel, decision of administrative-management matters, and use of material and financial resources.

It is imperative to make full use of the considerable scientific potential of Russian medical VUZ's to search for and develop promising ideas, gain new knowledge, and enhance the intellectual potential of medical science in the Russian Federation.

At this stage of development of medicine in Russia, special attention must be devoted to providing working conditions for talented scientists, authors of original

ideas and innovations, which would enable them to pursue independently work on scientific problems and given them the right not only to adequate working conditions, but also an equal right to the opportunity to prove the truth, and their approach to solving scientific problems.

Integration of the academic and VUZ sectors of Russian medical science must lead to: organization of special structures in scientific institutions of the Russian Academy of Medical Sciences for joint specialized training of scientific personnel; granting broad opportunities to scientists working at medical VUZ's of the Russian Federation, graduate students, trainees, students, scientific associates and specialists to make full use of the scientific and technical potential of the Russian Academy of Medical Sciences for carrying out research; establishment at medical universities and medical VUZ's of departments and faculties under the scientific control of Academy institutes, scientific institutions with dual subordination, interagency ad hoc scientific teams headed by active and corresponding members of the Russian Academy of Medical Sciences.

The general meeting of the Russian Academy of Medical Sciences expresses its alarm at the catastrophic situation that has developed in the area of publication of scientific medical periodicals, and believes that further development of medical science in the Russian Federation in the future is impossible, without taking speedy and radical steps to improve publishing work, and providing as a separate item starting with 1992, special allocations for publishing of Academy periodicals.

The general meeting of the Russian Academy of Medical Sciences is concerned by the worsening of the financial and material-technical support of research working conditions of scientists, their social protection, and believes that the Russian Academy of Medical Sciences will be unable to fully execute the functions imposed upon it to develop medical science in the Russian Federation without increasing by several times the budgeted allocations, including those in hard currency, for basic and applied research.

The general meeting of the Russian Academy of Medical Sciences puts to Academy management the task of obtaining from the government a considerable increase in budgeted financing of medical science in Russia with consideration of the changing price index, including achievement of an adequate financial situation for Academy personnel. The general meeting of the Russian Academy of Medical Sciences hereby decrees:

1. To confirm the complement of active and corresponding members of the Russian Academy of Medical Sciences.
2. To approve the text of an address to the administrators of the Commonwealth of Independent States, all political figures and people of good will.

3. To approve the draft of the Temporary Bylaws of the Russian Academy of Medical Sciences (RAMN) as the basis and confirm it as the Temporary Academy Bylaws, with amendments and additions.

4. To establish equal rights for all members of the Russian Academy of Medical Sciences regardless of membership to Commonwealth states in solving general and scientific problems, with the exception of elections of administrative bodies and new Academy members.

5. To approve the composition of a commission to work on the Bylaws of the Russian Academy of Medical Sciences and ask that it prepare (4th quarter of 1992) the following drafts for the approval of a general meeting of the Academy: Bylaws of the Russian Academy of Medical Sciences, Statute on the Basic Guidelines for Organizing Scientific Medical Research in the Russian Federation and the Structure of the Russian Academy of Medical Sciences, Statute on Scientific Research Institutions, providing for further democratization of activities of the academic community and greater independence of scientific institutions (appendix).

6. To support the proposals of scientists, specialists and the unanimous decision of the Bureau of the department of hygiene, microbiology and epidemiology of the Academy concerning change in name of the department and renaming it the department of preventive medicine of the Russian Academy of Medical Sciences.

7. To deem it desirable to have permanent and ad hoc scientific research groups for development of both research projects and different parts of national scientific programs within the structure of scientific institutions of the Russian Academy of Medical Sciences, in addition to laboratories and departments.

8. To develop scientific-production and commercial-entrepreneurial activities related to the sale of medical scientific and technical developments in the scientific institutions of the Russian Academy of Medical Sciences and medical VUZ's, and to help in the creation of small, science-oriented enterprises at scientific institutions and medical institutes.

9. To consider effective for the Russian Academy of Medical Sciences, as the successor of the USSR Academy of Sciences [AMN], the regulations and decrees of the presidium of the USSR AMN, bylaws of scientific research institutes if they are not in contradictions to the presidential ukases in effect in the Russian Federation and decrees of the Russian government, prior to approval of new decisions and implementation of the Basic Guidelines for Organization of Scientific Medical Research in the Russian Federation and Status of Scientific Research Institutes of the Russian Academy of Medical Sciences.

10. The presidium of the Russian Academy of Medical Sciences is instructed:

—to define the main directions of research in 1992 in scientific research institutions of the Russian Academy of

Medical Sciences and medical VUZ's, on the basis of analysis of the health status of the multinational people of the Russian Federation, in order to elaborate national and regional scientific-technical programs, with definition of the stages and conditions of their financing, as well as a list of scientific problems requiring solution on the national and regional levels;

—to implement measures for mandatory execution of Ukase No 5, dated 4 January 1992, of the president of the Russian Federation in the matter of financial and material-technical support of research, changes in wage conditions, social protection of scientists, relieving scientific institutions, organizations and enterprises of the Academy of taxes, collections and duty payments;

—to hold quarterly meetings of the board of directors of scientific institutions of the Russian Academy of Medical Sciences for the purpose of current discussion of scientific-organizational problems related to further development of medical science in the Russian Federation and enhancement of effectiveness of research and development;

—to prepare, during the 2d quarter of 1992, and approve a new structure for the system of the presidium of the Russian Academy of Medical Sciences;

—to reorganize (April 1992) the system of departments of the Russian Academy of Medical Sciences, providing for creation of independent sectors or sections for ongoing and more comprehensive forecasting, planning and coordination of research;

—to confirm, in April-May 1992, the new members of councils of experts of the Russian Academy of Medical Sciences for more judicious use of financial resources and material support of priority research and developments;

—to open, in the first semester of 1992, a section on planning and coordination of research at medical VUZ's of the Russian Federation within the Scientific Coordinating and Information Administration of the Russian Academy Medical Sciences;

—to attach the Tomsk Research Center to the Siberian Department of the Russian Academy of Medical Sciences, making it directly subordinated to this department;

—to develop, in 1992, several scientific and educational complexes in the Russian Federation, for the purpose of coordinating research carried out in scientific institutions of the Russian Academy of Medical Sciences and medical VUZ's of Russia;

—to organize, in the 4th quarter of 1992, a Far East Research Center of the Russian Academy of Medical Sciences;

—to activate work directly at scientific institutions of the Russian Academy of Medical Sciences and medical VUZ's, adopt the practice of regularly informing presidium members of the work done at scientific

research institutes, scientific developments of sections, laboratories, departments and individual researchers, and to provide them with methodological and financial assistance in organizing and carrying out research in priority directions of medical science;

—to address the Russian government with the request to assign special allocations for publication of Academy medical periodicals;

—to implement financing of publication of Academy medical periodicals by withholding a specific (needed) percentage of allocations from the annual budget of scientific institutions of the Russian Academy of Medical Sciences;

—to hold, in December 1992, an All-Russian conference of heads and deputy-heads dealing with scientific work at medical institutes on matters of further development of medical research and enhancement of effectiveness in utilizing the scientific potential of Russian Federation VUZ's;

—to restore (second semester of 1992) the previously existing Academic lecture series, "Forum of the Russian Academy of Medical Sciences," in the Russian Academy of Medical Sciences for the purpose of giving broad information to the public and medical community of Russia about the status of development, achievements of medical science, health care and dissemination of medical knowledge;

—to address editorial boards of mass media, radio and television of the Russian Federation with the request to provide the people of Russia with more objective, pondered and professionally literate information about the possibility and difficulties in solving different scientific and practical problems in the field of Russian medicine and health care, avoiding sensationalism and premature publication of factual material;

—to address (April 1992) administrators of the Commonwealth of Independent States and their governments with the suggestion to prepare and endorse a multilateral (bilateral) agreement, within the framework of the Commonwealth, concerning joint development, implementation and financing of targeted programs of greatest importance and problems in common with the Independent States of developing basic and applied research in the field of medical science and training highly qualified scientific personnel, establishing a Commonwealth council for medical science for collaboration in the fields of experimental, clinical and preventive medicine as needed to safeguard the health of the people.

11. Administrators of departments and structural entities of the Russian Academy of Medical Sciences should work on this decree during the 2d quarter of 1992, then submit their views concerning the system of organization and coordination of medical science in Russia, the draft of the RAMN Bylaws and tasks for the Academy.

12. Administrators of scientific groups, institutions, organizations and enterprises of the Russian Academy of Medical Sciences are instructed:

—to be governed in their work by the Temporary Academy Bylaws until the new Bylaws of the Russian Academy of Medical Sciences are approved;

—to routinely devote special attention to providing the necessary conditions for creative work of authors of original, progressive ideas and innovations, small scientific teams and individual researchers engaged in developing promising directions of medical science.

13. The second (65th) session of the general meeting of the Russian Academy of Medical Sciences should be scheduled in the 4th quarter of 1992 with the agenda: "Health Status of the People of the Russian Federation, and Basic Directions of Research in Institutions of the Russian Academy of Medical Sciences and Medical VUZ's of Russia," and "Neurosciences, Their Place and Role in Modern Medicine."

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### Medical Organizations Renamed

937C0138C Moscow VESTNIK ROSSIYSKOY  
AKADEMII MEDITSINSKIKH NAUK in Russian  
No 6, Jun 92 (signed to press 31 Jul 92) p 14

[Article by V. N. Pokrovskiy, president of the Russian Academy of Medical Sciences, academician of RAMN]

[Text] In accordance with Item 6 of the Decree of the First (64th) Session of the General Meeting of the Russian Academy of Medical Sciences on 24-25 March 1992, I hereby direct that:

1. The Department of Hygiene, Microbiology, and Epidemiology of the Russian Academy of Medical Sciences be renamed the Department of Preventive Medicine of the Russian Academy of Medical Sciences.

In accordance with Decree No 35 of the presidium of the Russian Academy of Medical Sciences dated 27 May 1992 "On Renaming Some Scientific Research Institutes in the Department of Preventive Medicine," I hereby direct that:

1. The Scientific Research Institute of Industrial Hygiene and Occupational Diseases of the Russian Academy of Medical Sciences be renamed the Scientific Research Institute of Industrial Medicine of the Russian Academy of Medical Sciences.

2. The Scientific Research Institute of General and Communal Hygiene imeni A. N. Sysin of the Russian Academy of Medical Sciences be renamed the Scientific Research Institute of Human Ecology and Environmental Hygiene imeni A. N. Sysin of the Russian Academy of Medical Sciences. ©Izdatelstvo "Meditsina", 1992

**Enzyme Immunoassay Test Systems for Identifying HIV Antigen and An Attempt To Use Them in Examining HIV-Infected Individuals**

937C0128A Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 [manuscript  
submitted 10 Jun 91] pp 444-447

[Article by G. R. Matsevich, A. I. Starov, S. S. Marenikova, O. G. Andzhaparidze, Scientific Research Institute of Viral Preparations, USSR Academy of Medical Sciences, Moscow; UDC 616.153.962.4-097:578.828.6]-078.333]

[Abstract] Today's test systems for the identification of HIV antibodies are inadequate in that they require additional verifying tests, such as immunoblotting. Since an alternative to the identification of HIV could be an enzyme immunoassay for identifying HIV antigens in clinical material, the researchers here chose to attempt to design antigen-based HIV-identification EIA variations that would have a high degree of sensitivity and specificity and would include a confirmatory test. They developed two tests, one using streptavidin-peroxidase complexes, the other using biotin- $\beta$ -lactamase enzyme complexes. The sensitivity of both tests rose considerably when immunoglobulins isolated from sera of various HIV patients were used to prepare the immunosorbent and the biotinylated antibodies. Sensitivity also rose when the contact between the virus-containing material and the immunosorbent was extended to 16-18 hours at room temperature, as opposed to 1-2 hours at 37-40°C. The two systems were sensitive enough to identify the antigen in the blood of 54-56 percent of HIV-infected individuals, as opposed to 60 percent in test systems by DuPont and Diagnostics Pasteur. Although the test involving  $\beta$ -lactamase was easier to read, the researchers preferred the streptavidin-peroxidase system because it was more stable, the enzyme complex was more uniform, and the test results were more reproducible. Figures 1, references 24: 3 Russian, 21 Western.

**Study of the Receptor Region of Venezuelan Equine Encephalitis With Monoclonal Antibodies**

937C0128B Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 [manuscript  
submitted 29 May 91] pp 489-492

[Article by I. A. Razumov, A. V. Pereboyev, Ye. V. Protopopova, A. D. Khusainova, Ye. V. Agapov, Ye. E. Melnikova, S. Ya. Gaydamovich, V. B. Loktev, All-Union Scientific Research Institute of Molecular Biology, NPO Vektor, concern Biopreparat, Novosibirsk; Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow; UDC 578.833.1:578.23].083.33]

[Abstract] Cell/ $\alpha$ -virus interactions depend largely on the receptor interaction that occurs between virion surface glycoproteins and the cell. It is clear that the heterodimer E1-E2 serves as the receptor, and it has been shown that

many types of monoclonal antibodies to the E1 protein of  $\alpha$ -viruses block the virions ability to induce hemagglutination of erythrocytes. The VEE virus has similar epitopes on protein E2. After producing a panel of monoclonal antibodies to the VEE virus and using them to refine the topology of antigen determinants of the E2 protein, the researchers here found that monoclonal antibodies to three E2 sites are capable of blocking the hemagglutination reaction. That prompted them to perform a more detailed study of the region. Seventeen hybridomas to VEE and EEE were selected for study. The monoclonal antibodies secreted by those lines were capable of blocking the hemagglutination reaction associated with VEE and EEE. All the antibodies interacted with the E2 protein, except for the EEE hybridoma 5H6. Three different sites on the VEE virus were found to block hemagglutination. Concurrent RIA was used to make preliminary site divisions of the EEE E2 protein. The researchers found that at least three non-overlapping sites on the EEE virus were associated with antihemagglutination activity. The data suggest that the region is rather large. Eight types of monoclonal antibodies were found to block hemagglutination in typical representatives of  $\alpha$ -viruses, i.e., VEE Trinidad and TC-83 strains, EEE southern and Virginia strains, WEE, Sindbis, Semiliki Forest, Pixun, and Chikungunya. The researchers hypothesized that the E2 glycoprotein has two regions: a variable region consisting of two sites, and a conservative region. Concurrent analysis demonstrated that the conservative region on the VEE virus is confined to one site, which includes six epitopes for binding monoclonal antibodies. The researchers feel that the conservative region supports the initial interaction of virus and cell, whereas the variable region determines the tissue tropism of the  $\alpha$ -viruses. References 27: 4 Russian, 23 Western.

**Course of Infection in Rabbits Contaminated With VEE by the Airborne Route**

937C0128C Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 (manuscript  
submitted 14 May 91) pp 492-495

[Article by A. N. Sergeyev, A. B. Ryzhikov, L. Ye. Bulychiev, Ye. O. Stepkina, N. V. Tkacheva, All-Union Scientific Research Institute, NPO Vektor, Novosibirsk; UDC 616.98:578.833.1]-092.9:599.325.1]-036]

[Abstract] The lack of information on airborne VEE infection of laboratory animals prompted the researchers here to study the clinical, virological, serological, and histological characteristics associated with airborne infection in Chinchilla rabbits. The animals were infected with the Trinidad strain in STW<sub>50</sub> doses of 4(2-8) PFU. Body temperature was noted to rise by at least 0.5°C within one or two days. Most of the animals died within 3-5 days, but death came in two waves for control animals (intravenously infected). The first wave occurred within 1-4 days, the second, within 5-8 days. The animals that had been infected through the respiratory tract also died primarily in two waves, which were



spaced closer together. The experimental rabbits that died in the first wave showed no symptoms until the fourth day and succumbed as a result of lymphoid tissue involvement. The experimental rabbits that died in the second wave probably died as a result of immunopathological response in the brain. Figures 1, references 7: 1 Russian, 6 Western.

### Biological and Immunochemical Properties of Monoclonal Antibodies to VEE Virus

937C0128D Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 (manuscript  
submitted 19 Nov 90) pp 495-498

[Article by M. V. Shpilevaya, Sh. M. Tugizov, A. A. Kushch, Ya. Ya. Tsilinskiy, N. Ye. Makarova, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow; UDC 616.98:578.833.26]-078.33]

[Abstract] The VEE virus contains the two structural glycoproteins E1 (50-53 kilodaltons) and E2 (56-59 kilodaltons). Glycoproteins are involved in the penetration of the virus into the cell and in the formation of antiviral immunity in an infected organism. Monospecific anti-E2 serum and monoclonal antibodies to E2 are known to neutralize the infectious and hemagglutinating activity of the VEE virus. Certain E1 epitopes also demonstrate virus-neutralizing activity and hemagglutination, albeit after a weaker fashion. In studying the properties of both glycoproteins, the researchers here produce five strains of hybrid cells that secrete VEE IgG monoclonal antibodies of two subclasses: IgG1 (VEE B5, VEE A4, VEE C6), and IgG2 (VEE A5, VEE G1). The VEE C6 antibodies are highly active in neutralization and hemagglutination and are directed to the E1 critical site that takes part in the adsorption of the virus on sensitive cells and in the neutralization of the infectious activity. The site with which VEE A5 interacts is not overlapped by the first site and has no effect on viral infection capacity or hemagglutination. VEE A4 and VEE B5 are conformationally dependent and demonstrate hemagglutination activity. Figures 2, references 15: 1 Russian, 14 Western.

### Comparative Study of the Interaction of Marburg Virus and Macrophages of Various Species of Animals In Vitro

937C0128E Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 (manuscript  
submitted 18 Jun 91) pp 503-506

[Article by A. A. Skripchenko, A. M. Shestopalov, O. Ya. Yaroslavl'tseva, All-Union Scientific Research Institute, NPO Vektor, Novosibirsk; UDC 616.98:578.824]-07:616.155.33]-092.9]

[Abstract] Macrophages, which are a necessary component of nonspecific protection against viral infection, can themselves be damaged by a virus and thus serve as

a primary focus for viral reproduction. Interested in comparing the ability of peritoneal macrophages to support Marburg virus reproduction in vitro and the adsorption capacity of the virus, the researchers here studied the reproduction of the virus in sensitive and resistant animal species: chinchilla rabbits, guinea pigs, green monkeys, rhesus monkeys, and hamadryad baboons. They ultimately placed the animals into three groups, depending on the how well the virus was supported in the peritoneal macrophages of the species. The guinea pigs and the green monkeys—both sensitive to the virus—made up the first group (5.58 and 5.51 log PFU/ml virus, respectively, with viral reproduction peak at 5-6 days). The baboons and the rhesus monkeys formed the second group (baboons, 5.66 log PFU/ml, but only after nine days; rhesus, 3.30 after eight days). The chinchilla rabbits, which were not sensitive to the virus, made up the third group. Human sensitivity to the virus was studied with a population of peripheral blood cells 90 percent of which were monocytes (5.67 log PFU/ml, after nine days). Macrophages of all the species studied adsorb the Marburg virus. It was found, however, that the number of such macrophages drops sharply in immune guinea pigs and green monkeys. References 20: 1 Russian, 19 Western.

### Experimental Study of Transmission of Marburg Virus Through Contact

937C0128F Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 (manuscript  
submitted 6 May 91) pp 506-508

[Article by V. A. Pokhodyayev, N. I. Gonchar, V. A. Pshenichnov, Scientific Research Institute of Microbiology, USSR Ministry of Defense, Zagorsk; UDC 578.824:578.42]

[Abstract] The Popp strain of the Marburg virus was used in a study of the transmission of the virus via contact in guinea pigs and rhesus monkeys. Certain of the guinea pigs were infected intraperitoneally with a 1000 LD<sub>50</sub> dose and were kept with healthy guinea pigs for 12-60 hours. Exposure was planned for the end of the incubation period and the beginning of symptoms. The percentage of animals that became infected through the contact grew with exposure to the sick animals, as did the lifespan after exposure. Healthy monkeys were kept with infected monkeys (1-100 LD<sub>50</sub> subcutaneously or intranasally) or on a level that was 1.5 meters above the infected monkeys (no physical contact). Exposure was during the clinical infection stage. Rate of infection among the monkeys was considerably higher than among the guinea pigs. Although the rate of secondary infection among the monkeys isolated from physical contact was lower than among those in direct contact with the sick monkeys, the airborne route of infection was proved possible. References 10: 2 Russian, 8 Western.



**Monoclonal Antibodies to Machupo Virus:  
Production and Preliminary Description**

937C0128G Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 [manuscript  
submitted 10 Jun 91] pp 508-511

[Article by I. V. Malakhova, L. Ya. Kunitskaya, L. Ye. Surikova, S. I. Bystrova, T. V. Shkolina, A. S. Vladyko, Belorussian Scientific Research Institute of Epidemiology and Microbiology, BSSR Ministry of Health, Minsk; UDC 616.98:578.833.29]-078.33]

[Abstract] Machupo virus is a pathogenic representative of a family of arenaviruses and results in Bolivian hemorrhagic fever, which is fatal in 19-40 percent of cases. Because the literature contained no information on the use of monoclonal antibodies to the Machupo virus to identify antigenic cross-reactivity among viruses of the Tacaribe complex, the researchers set out to create hybridomas that would produce monoclonal antibodies to the Machupo virus. After working out a suitable schedule for immunizing BALB/c mice to produce hyperimmune animals, they hybridized myeloma cells of mice with immune splenocytes based on X-63, FG, and NS-1 cells. Ten positive clones were produced on the basis of the NS-1 cells. All the resulting hybridomas were found to produce G1 immunoglobulins. The monoclonal antibodies precipitated one viral protein with a molecular weight of 68 kilodaltons (nucleocapsid protein). Ascitic tumors containing monoclonal antibodies to the Machupo virus were induced, and then hybrid cells producing such antibodies were cloned. Most of the monoclonal antibodies interact with the heterologous Lassa arenavirus in indirect immunofluorescence. In a study of interaction with the Tacaribe and Tamiami arenaviruses, the monoclonal antibody 3140 revealed a specific cytoplasmic fluorescence with both the viruses. All the monoclonal antibodies studied here, with the exception of 3101, demonstrated a broad spectrum of heterologous activity and were capable of identifying general antigen determinants for most arenaviruses. Antigen cross-reactivity between the Machupo and Lassa viruses was identified by the antibodies 3103, 3106, 3107, 3122, 3140. Figures 1, references 14: 5 Russian, 9 Western.

**Effectiveness of Immobilized Liposomal  
Preparations of Ribamidyl in Experimental Rift  
Valley Fever**

937C0128H Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 6, Nov-Dec 91 (manuscript  
submitted 6 May 91) pp 512-514

[Article by L. P. Grabareva, R. A. Khamitov, V. A. Pshenichnov, Scientific Research Institute of Microbiology, USSR Ministry of Defense, Zagorsk; UDC 616.98:578.833.1]-092.9-085.281.8]

[Abstract] The isolation of the Rift Valley Fever virus in Afghanistan makes the creation of an effective treatment for the fever an urgent problem in the former Soviet

Union. Little is known of the stability of liposomal preparations in the body, of their interaction with cells, or of the complexity of the production of standard liposomal preparations with an antiviral component. In an experimental study of liposome-immobilized ribamidyl—an analog of ribavirin—the researchers found that the effectiveness of the immobilization of drugs in liposomes depends largely on the volume of water enclosed, on the basis of which they hypothesize that increasing the ribamidyl content could stabilize the liposome by producing a denser packing of the carbohydrate chains in the lipid membranes. They found the experimental immobilized ribamidyl to be more effective than free ribamidyl in terms of the survivability of white mice after infection with doses of 25-50 PFU (the mice administered the immobilized ribamidyl survived twice as long). Both, however, produced similar times, and both reduced viral concentration in the livers of the infected mice by day three. White rats infected with doses of 250 PFU also demonstrated survival rates that were twice as high as control. When the infecting dose is raised to 5,000 PFU, free ribavirin assumes the role of the more effective treatment. References 8: 4 Russian, 4 Western.

**Comparison of Heterogeneity of GMK-AH-1 Cell  
Culture and Stability of Rift Valley Fever Virus  
Plaque Formation in It**

937C0129A Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 1, Nov-Dec 91 p 529

[Article by V. T. Lyamar, M. R. Yalyshev, and O. A. Lomachenkova; UDC 57.085.23:576.316.23]

[Text] With the objective of studying the conventionality of a continuously passed cell culture with respect to the functional status of nucleolus-shaped regions (NSR), we investigated the stability of NSR in cultures of GMK-AH-1 and its clones. This analysis made it possible to establish that in the original population and in the clones, the quantitative characteristics of the modal class are stable throughout long-term cultivation. Data on the distribution of the proportion of cells within the modal class show that its variability in the clones is narrower than in the original population. The NSR is located in the marker chromosomes with pronounced secondary overwind. The variability of the indexes of the frequency of the markers and the degree of staining of the homologs during long-term cultivation remains within 1-2 percent. Results of researching the stability of the modal class indexes of the populations agree with data on NSR stability. Along with studying the genome of the populations, we researched their virus-producing ability when infected with Rift Valley fever virus. Each population of cells has its own level of characteristics that are stable throughout the cultivation period. The results indicate the stability of the NSR chromosomes of the original cell culture and its clones during long term cultivation in strictly defined maintenance conditions; the "trueness" of the resultant clones; and the possibility of using data on the functional condition of the NSR as an indicator of

virus production by the cell cultures. Tables 3; References 10 (manuscript deposited at the All-Union Institute of Scientific and Technical Information, 5 April 1991, No 1460.B).

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937C0129B Moscow VOPROSY VIRUSOLOGII  
in Russian Vol 36 No 1, Nov-Dec 91 p 530

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